

=> fil reg

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STRUCTURE FILE UPDATES: 3 APR 2001 HIGHEST RN 329897-04-3
 DICTIONARY FILE UPDATES: 3 APR 2001 HIGHEST RN 329897-04-3

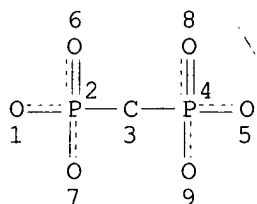
TSCA INFORMATION NOW CURRENT THROUGH July 8, 2000

Please note that search-term pricing does apply when
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Structure search limits have been increased. See HELP SLIMIT
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=> d sta que 16

L1 STR

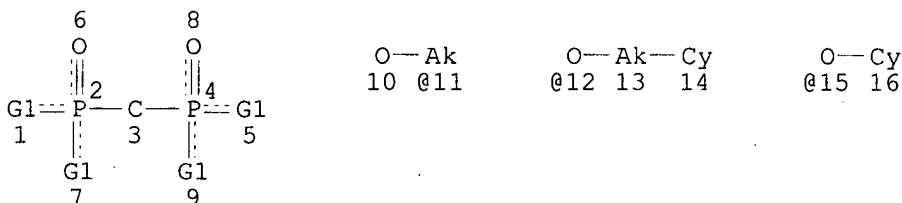


Point of Contact:
 Jan Delaval
 Librarian-Physical Sciences
 CM1 1E01 Tel: 308-4498

NODE ATTRIBUTES:
 DEFAULT MLEVEL IS ATOM
 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
 RING(S) ARE ISOLATED OR EMBEDDED
 NUMBER OF NODES IS 9

STEREO ATTRIBUTES: NONE
 L3 9837 SEA FILE=REGISTRY SSS FUL L1
 L4 STR



VAR G1=OH/11/15/12

NODE ATTRIBUTES:
 DEFAULT MLEVEL IS ATOM
 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
 RING(S) ARE ISOLATED OR EMBEDDED
 NUMBER OF NODES IS 16

STEREO ATTRIBUTES: NONE
 L6 5983 SEA FILE=REGISTRY SUB=L3 SSS FUL L4

100.0% PROCESSED 9837 ITERATIONS
 SEARCH TIME: 00.00.10

5983 ANSWERS

=> d his 16-

(FILE 'REGISTRY' ENTERED AT 09:54:49 ON 04 APR 2001)

L6 5983 S L4 FUL SUB=L3
SAV L6 KWON7199A/A

L7 411 S L6 AND (ADEN? OR GUAN? OR THYM? OR CYTID? OR URAC?)

L8 5572 S L6 NOT L7

FILE 'HCAPLUS' ENTERED AT 10:07:04 ON 04 APR 2001

L9 6750 S L8

L10 235 S L7

FILE 'REGISTRY' ENTERED AT 10:07:38 ON 04 APR 2001

L11 3854 S L3 NOT L6-L8

FILE 'HCAPLUS' ENTERED AT 10:07:51 ON 04 APR 2001

L12 2446 S L11
E AUTOIMMUN/CW

L13 5718 S E4,E5
E AUTOIMMUN/CT
E E9+ALL

L14 12099 S E3,E2+NT
E AUTOIMMUNI/CT
E E4+ALL

L15 936 S E1,E2

L16 672 S HASHIMOT? (L) THYROID?

L17 1993 S MYASTHEN? (L) GRAV?

L18 6961 S LUPUS (L) ERYTHEMAT?
E LUPUS/CT
E E9+ALL

L19 5510 S E5,E4+NT
E HASHIMOTO/CW
E THYROIDITIS/CW

L20 130 S E3
E THYROIDITIS/CT
E E3+ALL

L21 367 S E2
E MYASTHEN/CW

L22 1648 S E4
E MYASTHEN/CT
E E5+ALL

L23 1648 S E5
E DIABETES MELLITUS/CT
E E3+ALL

L24 37888 S E4+NT

L25 42636 S DIABET? (L) MELLIT?

L26 14201 S DIABET? (L) INSULIN (L) DEPEND?

L27 1027 S PRIMARY (L) BILIAR? (L) CIRRHOS?
E PRIMARY BILIARY/CT
E E4+ALL

L28 406 S E1,E2
E CIRRHOSIS/CW

L29 486 S E3 (L) BILIAR?
E CIRRHOSIS/CT
E E5+ALL

L30 342 S E6,E5
E CIRRHOSIS/CT
E E3+ALL

L31 42 S E5,E6 (L) BILIAR?

L32 11494 S HEPAT? (L) CHRONIC
E HEPATITIS/CW

L33 2496 S E3 (L) CHRONIC
E HEPATITIS/CT
E EE16+ALL

		E HEPATITIS/CT
		E E16+ALL
L34	32	S E2
L35	225	S E1
		E HEPATITIS/CT
		E E3+ALL
L36	2385	S E6+NT (L) CHRONIC
L37	655	S E11-E14
L38	537	S ADDISON? (L) (DISEASE OR DISORDER OR SYNDROM?)
		E ADDISON/CT
		E E5+ALL
L39	307	S E5
L40	52	S HYPOADRENOCORT?
L41	431	S POLYMYOSIT? OR POLY MYOSIT?
		E POLYMYOSIT/CW
L42	77	S E4
		E POLYMYOSIT/CT
		E E4+ALL
L43	215	S E2, E1
		E DERMATOMYOSIT/CW
L44	234	S E4
		E DERMATOMYOSIT/CT
		E E4+ALL
L45	234	S E9
L46	345	S DERMATOMYOSIT?
L47	557	S AUTOIMMUN? (L) (ANEMI? OR ANAEMI?)
L48	414	S AUTOIMMUN? (L) (ANEMI? OR ANAEMI?) (L) (HAEMOLYT? OR HEMOLYT?)
		E ANEMI/CT
		E E5+ALL
L49	686	S E4 (L) (HEMOLYT? OR HAEMOLYT?)
L50	612	S E3 (L) (HEMOLYT? OR HAEMOLYT?)
L51	94	S E11
L52	710	S E3+NT (L) (HEMOLYT? OR HAEMOLYT?)
L53	1194	S MYOCARDIT?
		E MYOCARDIT?/CW
L54	178	S E4
		E MYOCARDIT?/CT
		E E4+ALL
L55	354	S E2
L56	178	S E1
		E MYOCARDIT?/CT
		E E6+ALL
L57	91	S E1, E2
		E MYOPERICARDIT/CW
L58	2	S MYOPERICARDIT?
		E PERICARDIUM/CW
L59	46	S E3 (L) PERICARDIT?
		E SCLERODERM/CW
L60	306	S E4
		E SCLERODERM/CT
		E E5+ALL
L61	812	S E2
		E SCLERODERM/CT
		E E4+ALL
L62	259	S E1
L63	1608	S SCLERODERM?
		E UVEITIS/CW
L64	155	S E3
		E UVEITIS/CT
		E E3+ALL
L65	475	S E1, E2
		E UVEITIS/CT
		E E4+ALL
L66	62	S E2
L67	1024	S UVEITI?
		E PHACOUVEIT/CW

L68 0 S PHACOUVEIT?
 L69 0 S ?COUVEIT?
 E OPHTALMIA/CW
 L70 0 S OPHTALMIA
 L71 49 S OPHTHALMIA
 E OPHTHALMIA/CW
 L72 310 S PEMPHIG? (L) VULGAR?
 E PEMPHIG/CW
 L73 2 S E6,E7 (L) VULGAR?
 E PEMPHIG/CT
 E E10+ALL
 L74 114 S E1,E2
 E PEMPHIGUS VULGARIS/CT
 E E4+ALL
 L75 579 S PEMPHIGOID
 E PEMPHIGOID/CW
 L76 49 S E3
 E PEMPHIGOID/CT
 E E4+ALL
 L77 161 S E2
 L78 594 S PERNICI? (L) (ANEMI? OR ANAEMI?)
 E ANEMI/CW
 L79 307 S E4 (L) PERNIC?
 E ANEMI/CT
 E E5+ALL
 L80 307 S E4,E3+NT (L) PERNIC?
 L81 726 S ATROPH? (L) GASTRI?
 E ATROPHIC/CT
 E E4+ALL
 L82 58 S E2
 E GASTRI/CT
 L83 51 S GASTR?/CW (L) ATROPH?
 L84 154 S STOMACH?/CW (L) ATROPH?
 L85 131 S L84 (L) GASTR?
 L86 2435 S CROHN? (L) (DISEASE OR DISORDER OR SYNDROM?)
 E CROHN/CW
 L87 526 S E3
 E CROHN/CT
 E E6+ALL
 L88 526 S E1,E2
 L89 2770 S (COLIC OR COLIT?) (L) ULCER?
 E COLIT/CW
 L90 568 S E4 (L) ULCER?
 E COLIT/CT
 E E4+ALL
 L91 1875 S E2,E1
 E ULCER/CT
 E E3+ALL
 L92 2 S E3,E2 (L) (COLIT? OR COLIC)
 L93 38065 S ALLERG?
 L94 545 S HAYFEVER OR HAY FEVER
 L95 10105 S POLLEN
 E ALLERG/CW
 L96 24554 S E4-E6,E8
 E ALLERG/CT
 E E6+ALL
 L97 5804 S E3
 E E7+ALL
 L98 15176 S E3,E4,E2+NT
 E E26+ALL
 L99 517 S E4
 L100 23883 S AUTOIMMUN? OR AUTO IMMUN?
 E IMMUN/CW
 L101 1379 S E4,E6 (L) AUTO
 L102 59 S L9 AND L13-L101
 L103 0 S L10 AND L13-L101

L104 15 S L11 AND L13-L101
L105 70 SS L102,L104
E JOMAA H/AU
L106 26 S E3,E4
L107 2 S L106 AND L13-L101
L108 2 S L106 AND L9,L10,L12
L109 3 S L107,L108
L110 6291 S MULTIP? (L) SCLEROS?
E MULTIPLE SCLER/CT
E E4+ALL
L111 4389 S E3+NT
E SCLERO/CT
E E112+ALL
L112 1819 S E2,E1
L113 472 S E1,E2 (L) MULTIPL?
L114 4 S L9,L10,L12 AND L110-L113
L115 70 S L105,L114
L116 1 S L106 AND L110-L113
L117 3 S L109,L116
L118 72 S L115,L117
L119 51 S L115 AND (PD<=19980626 OR PRD<=19980626 OR AD<=19980626 OR PY
L120 36 S L119 AND (1 OR 63 OR 15)/SC
L121 21 S L119 AND (1 OR 63 OR 15)/SX
L122 46 S L120,L121
L123 5 S L119 NOT L122
L124 3 S L123 NOT (8 OR 5)/SC
L125 49 S L122,L124
L126 1104 S L9 (L) THU/RL
L127 6 S L10 (L) THU/RL
L128 87 S L12 (L) THU/RL
L129 29 S L125 AND L126-L128
L130 9 S L129 AND (AUTOIMMUN? OR IMMUNITY OR IMMUNE)/CW
L131 7 S L129 AND (MATRIX OR SH2 OR PACLITAXEL OR COLLAGEN OR TOLERAB?
L132 22 S L129 NOT L131
L133 22 S L130,L132
L134 20 S L125 NOT L127-L133
L135 9 S L134 AND (RHENIUM OR COLLAGENASE OR ENDOTOXIN OR ATP OR BLADD
L136 11 S L134 NOT L135
L137 35 S L117,L133,L136
SEL HIT RN

FILE 'REGISTRY' ENTERED AT 11:02:57 ON 04 APR 2001
L138 62 S E1-E63
SAV L138 KWON7199B/A

← hits for L137

FILE 'REGISTRY' ENTERED AT 11:03:49 ON 04 APR 2001

=> fil hcaplus

FILE 'HCAPLUS' ENTERED AT 11:04:10 ON 04 APR 2001
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FILE COVERS 1967 - 4 Apr 2001 VOL 134 ISS 15
FILE LAST UPDATED: 3 Apr 2001 (20010403/ED)

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Now you can extend your author, patent assignee, patent information, and title searches back to 1907. The records from 1907-1966 now have this searchable data in CAOLD. You now have electronic access to all of CA: 1907 to 1966 in CAOLD and 1967 to the present in HCAPLUS on STN.

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L137 ANSWER 1 OF 35 HCAPLUS COPYRIGHT 2001 ACS

AN 2000:347 HCAPLUS

DN 132:59143

TI Use of bisphosphonates for the prophylaxis and treatment of infectious processes in humans and animals and for herbicides

IN Jomaa, Hassan

PA Germany

SO Ger. Offen., 8 pp.

CODEN: GWXXBX

DT Patent

LA German

IC ICM A61K031-66

CC 1-5 (Pharmacology)

Section cross-reference(s): 5

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 19859668	A1	19991230	DE 1998-19859668	19981223
	WO 2000038660	A2	20000706	WO 1999-EP10350	19991223
	WO 2000038660	A3	20001221		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI DE 1998-19827986 19980624

DE 1998-19859668 19981223

OS MARPAT 132:59143

AB Bisphosphonates are disclosed for the prophylaxis and treatment of infectious processes in humans and animals which are caused by viruses, bacteria, fungi, or parasites, and as a herbicide for plants.

ST antiinfective herbicide bisphosphonate; bactericide virucide fungicide parasiticide bisphosphonate

IT Trypanosoma cruzi

(Chagas' disease from; bisphosphonates for prophylaxis and treatment of infectious processes in humans and animals and for herbicides)

IT Cryptosporidium

(Cryptosporidiosis; bisphosphonates for prophylaxis and treatment of infectious processes in humans and animals and for herbicides)

IT Sarcocystis

(Sarcocystosis; bisphosphonates for prophylaxis and treatment of infectious processes in humans and animals and for herbicides)

IT Balantidium

(balantidiosis; bisphosphonates for prophylaxis and treatment of infectious processes in humans and animals and for herbicides)

IT Acanthamoeba

Actinobacillus

Actinomyces

Actinomycetaceae

Adenoviridae
Aeromonas
Aeromonas salmonicida
Alphavirus
Anti-infective agents
Antibacterial agents
Antimalarials
Antiviral agents
Aphthovirus
Arenaviridae
Arenavirus
Aviadenovirus
Avipoxvirus
BK virus
Bartonellaceae
Bordetella
Borrelia
Borrelia burgdorferi
Brucella
Bunyaviridae
Bunyavirus
Caliciviridae
Campylobacter
Campylobacter coli
Campylobacter fetus
Campylobacter jejuni
Capripoxvirus
Chlamydia psittaci
Chlamydia trachomatis
Chlamydiaceae
Clostridium
Coccidiosis
Coronaviridae
Corynebacterium
Corynebacterium diphtheriae
Corynebacterium pseudotuberculosis
Cytomegalovirus
Densovirus
Dependovirus
Dermatophilus
Ebola virus
Enterovirus
Erysipelothrix rhusiopathiae
Filoviridae
Flaviviridae
Flavivirus
Fungicides
Giardia
Giardia lamblia
Hantavirus
Helicobacter
Helicobacter pylori
Hepadnaviridae
Hepatitis A virus
Hepatitis B virus
Hepatitis C virus
Hepatitis E virus
Hepatitis F virus
Hepatitis G virus
Hepatitis delta virus
Hepatitis virus
Herbicides
Herpesviridae
Human T-lymphotropic virus
Human coxsackievirus
Human echovirus

Human herpesvirus
Human herpesvirus 3
Human herpesvirus 4
Human herpesvirus 6
Human herpesvirus 7
Human herpesvirus 8
Human immunodeficiency virus
Human poliovirus
Influenza virus
JC virus
Legionella
Legionellaceae
Lentivirus
Leporipoxvirus
Leptospira
Leptospiraceae
Listeria
Listeria monocytogenes
Listonella anguillarum
Lymphocytic choriomeningitis virus
Lyssavirus
Marburg virus
Mastadenovirus
Measles virus
Miopapovavirus
Molluscum contagiosum virus
Moraxella
Moraxella bovis
Morbillivirus
Mumps virus
Mycobacteriaceae
Mycobacterium avium
Mycoplasma
Mycoplasma pneumoniae
Mycoplasmataceae
Naegleria
Nairovirus
Neisseria
Neisseria gonorrhoeae
Neisseria meningitidis
Neisseriaceae
Nocardia
Orbivirus
Orthomyxoviridae
Orthopoxvirus
Papillomavirus
Papovaviridae
Paramyxoviridae
Paramyxovirus
Parapoxvirus
Parasiticide
Parvoviridae
Parvovirus
Pestivirus
Phlebovirus
Photobacterium
Picornaviridae
Plesiomonas
Pneumovirus
Polyomavirus
Poxviridae
Prion
Propionibacteriaceae
Propionibacterium
Propionibacterium acnes
Rabies virus

Reoviridae
 Retroviridae
 Rhabdoviridae
 Rhinovirus
 Rhodococcus
 Rickettsiaceae
 Rotavirus
 Rubella virus
 Rubivirus
 Spirochaetaceae
 Spumavirus
 Tick-borne encephalitis virus
 Togaviridae
 Treponema
 Trichomonacides
 Ureaplasma
 Uukuniemi virus
 Vesicular stomatitis virus
 Vibrio
 Vibrio cholerae
 Vibrionaceae
 Yersinia
 Yersinia enterocolitica
 Yersinia pestis
 Yersinia pseudotuberculosis
 Yersinia ruckeri

(bisphosphonates for prophylaxis and treatment of infectious processes in humans and animals and for herbicides)

- IT Virus
(hepatotropic; bisphosphonates for prophylaxis and treatment of infectious processes in humans and animals and for herbicides)
- IT Entamoeba
(infestation with, Dysentery, amebic; bisphosphonates for prophylaxis and treatment of infectious processes in humans and animals and for herbicides)
- IT Leishmania
(leishmaniasis from; bisphosphonates for prophylaxis and treatment of infectious processes in humans and animals and for herbicides)
- IT RNA viruses
(oncogenic; bisphosphonates for prophylaxis and treatment of infectious processes in humans and animals and for herbicides)
- IT Virus
(oncovirus; bisphosphonates for prophylaxis and treatment of infectious processes in humans and animals and for herbicides)
- IT Functional groups
(phosphonate group; bisphosphonates for prophylaxis and treatment of infectious processes in humans and animals and for herbicides)
- IT Pneumonia
(pneumocytosis; bisphosphonates for prophylaxis and treatment of infectious processes in humans and animals and for herbicides)
- IT Infection
(sleeping sickness; bisphosphonates for prophylaxis and treatment of infectious processes in humans and animals and for herbicides)
- IT Toxoplasma gondii
(toxoplasmosis from; bisphosphonates for prophylaxis and treatment of infectious processes in humans and animals and for herbicides)
- IT 13598-36-2D, Phosphonic acid, bisphosphonate derivs. 40391-99-9
40391-99-9D, derivs. 41003-10-5 41003-10-5D,
derivs. 66376-36-1 66376-36-1D, derivs.
79778-41-9 79778-41-9D, derivs. 89130-99-4
89130-99-4D, derivs. 89987-06-4 89987-06-4D,
derivs. 105462-23-5 105462-23-5D, derivs.
114084-78-5 114084-78-5D, derivs. 118072-93-8
118072-93-8D, derivs. 124351-85-5 124351-85-5D
, derivs. 253265-92-8 253265-92-8D, derivs.
RL: AGR (Agricultural use); BAC (Biological activity or effector, except

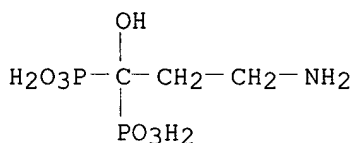
adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bisphosphonates for prophylaxis and treatment of infectious processes
in humans and animals and for herbicides)

IT 40391-99-9

RL: AGR (Agricultural use); BAC (Biological activity or effector, except
adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bisphosphonates for prophylaxis and treatment of infectious processes
in humans and animals and for herbicides)

RN 40391-99-9 HCAPLUS

CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis- (9CI) (CA INDEX NAME)



L137 ANSWER 2 OF 35 HCAPLUS COPYRIGHT 2001 ACS

AN 2000:301 HCAPLUS

DN 132:69329

TI Medicaments containing bisphosphonic acids and their derivatives for
prophylaxis and treatment of **autoimmune** diseases and
allergies

IN Jomaa, Hassan

PA Germany

SO Ger. Offen., 10 pp.

CODEN: GWXXBX

DT Patent

LA German

IC ICM C07F009-40

ICS C07F009-58; C07F009-6506; A61K031-66; A61K031-675; A61K045-00

CC 63-6 (Pharmaceuticals)

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 19828450	A1	19991230	DE 1998-19828450	19980626 <--
	WO 2000000182	A2	20000106	WO 1999-DE1844	19990624 <--
	WO 2000000182	A3	20000330		
	W:	AL, AU, BB, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LK, LT, LV, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE			
	AU 9955033	A1	20000117	AU 1999-55033	19990624 <--
PRAI	DE 1998-19828450		19980626 <--		
	WO 1999-DE1844		19990624		

OS MARPAT 132:69329

AB Bisphosphonic acids and their derivs. A3OP(O)(OA4)CR1(XR2)P(O)(OA1)OA2
[A1-A4 = H, (substituted) alkyl, (substituted) aryl, (substituted)
aralkyl, (substituted) cycloalkyl, (substituted) heterocyclyl, metal of
groups IA, IIA, or IIIA, (substituted) ammonium; X = bond, alkylene,
alkenylene, hydroxyalkylene; R1, R2 = H, OH, NH2, (substituted) acyl,
(substituted) alkyl, (substituted) aryl, (substituted) cycloalkyl,
(substituted) aralkyl, (substituted) heterocyclyl, Cl, SR3, NR3R4; R3, R4
= H, OH, NH, (substituted) acyl, (substituted) alkyl, (substituted) aryl,
(substituted) cycloalkyl, (substituted) aralkyl, (substituted)
heterocyclyl], as well as their salts, esters, and prodrugs, in
combination with the appropriate autoantigens or **allergens** or
their fragments, derivs., or analogs thereof, are useful for reinduction
of immune tolerance to autoantigens and **allergens**, and thus for
prophylaxis and treatment of **autoimmune** diseases and
allergies. The bisphosphonate and the autoantigen or
allergen may be administered simultaneously or sequentially.

- Thus, tablets for treatment of **multiple sclerosis** contained di-Na 3-amino-1-hydroxypropylidene-1,1-bisphosphonate 600, myelin basic protein 8, mannitol 400, starch 50, and Mg stearate 10 mg.
- ST **autoimmune** disease treatment bisphosphonate autoantigen;
allergy inhibitor bisphosphonate **allergen**; immune tolerance induction bisphosphonate autoantigen
- IT **Intestine, disease**
 (Crohn's; medicaments contg. bisphosphonic acids and their derivs. for prophylaxis and treatment of **autoimmune diseases and allergies**)
- IT **Stomach, disease**
 (atrophic gastritis, **autoimmune**; medicaments contg. bisphosphonic acids and their derivs. for prophylaxis and treatment of **autoimmune diseases and allergies**)
- IT DNA
 Myelin basic protein
 RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (autoantigen; medicaments contg. bisphosphonic acids and their derivs. for prophylaxis and treatment of **autoimmune diseases and allergies**)
- IT Adrenal cortex
 Heart
 Hematopoietic precursor cell
 Intestine
 Liver
 Muscle
 Nervous system
 Pancreatic islet of Langerhans
 Skin
 Stomach
 (autoantigens of; medicaments contg. bisphosphonic acids and their derivs. for prophylaxis and treatment of **autoimmune diseases and allergies**)
- IT Antigens
 Arrestins
 Cholinergic receptors
 Intrinsic factors
 Thyroglobulin
 RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (autoantigens; medicaments contg. bisphosphonic acids and their derivs. for prophylaxis and treatment of **autoimmune diseases and allergies**)
- IT **Stomach, disease**
 (**autoimmune gastritis, atrophic**; medicaments contg. bisphosphonic acids and their derivs. for prophylaxis and treatment of **autoimmune diseases and allergies**)
- IT **Anemia (disease)**
 (**autoimmune hemolytic anemia**; medicaments contg. bisphosphonic acids and their derivs. for prophylaxis and treatment of **autoimmune diseases and allergies**)
- IT **Thyroid gland, disease**
 (**autoimmune thyroiditis**; medicaments contg. bisphosphonic acids and their derivs. for prophylaxis and treatment of **autoimmune diseases and allergies**)
- IT **Eye, disease**
 (**autoimmune uveitis**; medicaments contg. bisphosphonic acids and their derivs. for prophylaxis and treatment of **autoimmune diseases and allergies**)
- IT Drug delivery systems
 (capsules; medicaments contg. bisphosphonic acids and their derivs. for prophylaxis and treatment of **autoimmune diseases and allergies**)

- IT Drug delivery systems
(inhalants; medicaments contg. bisphosphonic acids and their derivs.
for prophylaxis and treatment of **autoimmune** diseases and
allergies)
- IT Eye
(lens, autoantigens of; medicaments contg. bisphosphonic acids and
their derivs. for prophylaxis and treatment of **autoimmune**
diseases and **allergies**)
- IT **Addison's disease**
Allergy inhibitors
Antidiabetic agents
Antirheumatic agents
Autoimmune disease
Dermatomyositis
Lupus erythematosus
Multiple sclerosis
Myasthenia gravis
(medicaments contg. bisphosphonic acids and their derivs. for
prophylaxis and treatment of **autoimmune diseases**
and **allergies**)
- IT **Allergens**
RL: BAC (Biological activity or effector, except adverse); THU
(Therapeutic use); BIOL (Biological study); USES (Uses)
(medicaments contg. bisphosphonic acids and their derivs. for
prophylaxis and treatment of **autoimmune** diseases and
allergies)
- IT **Heart, disease**
(**myocarditis**; medicaments contg. bisphosphonic acids and
their derivs. for prophylaxis and treatment of **autoimmune**
diseases and **allergies**)
- IT Drug delivery systems
(ointments; medicaments contg. bisphosphonic acids and their derivs.
for prophylaxis and treatment of **autoimmune** diseases and
allergies)
- IT Stomach
(parietal cell, autoantigens of; medicaments contg. bisphosphonic acids
and their derivs. for prophylaxis and treatment of **autoimmune**
diseases and **allergies**)
- IT **Skin, disease**
(**pemphigoid**; medicaments contg. bisphosphonic acids and their
derivs. for prophylaxis and treatment of **autoimmune** diseases
and **allergies**)
- IT **Skin, disease**
(**pemphigus vulgaris**; medicaments contg.
bisphosphonic acids and their derivs. for prophylaxis and treatment of
autoimmune diseases and **allergies**)
- IT **Pericardium**
(**pericarditis**; medicaments contg. bisphosphonic acids and
their derivs. for prophylaxis and treatment of **autoimmune**
diseases and **allergies**)
- IT **Anemia (disease)**
(**pernicious anemia**; medicaments contg.
bisphosphonic acids and their derivs. for prophylaxis and treatment of
autoimmune diseases and **allergies**)
- IT **Muscle, disease**
(**polymyositis**; medicaments contg. bisphosphonic acids and
their derivs. for prophylaxis and treatment of **autoimmune**
diseases and **allergies**)
- IT **Biliary tract**
(**primary biliary cirrhosis**; medicaments
contg. bisphosphonic acids and their derivs. for prophylaxis and
treatment of **autoimmune** diseases and **allergies**)
- IT **Connective tissue**
(**scleroderma**; medicaments contg. bisphosphonic acids and
their derivs. for prophylaxis and treatment of **autoimmune**
diseases and **allergies**)

- IT Drug delivery systems
(solids; medicaments contg. bisphosphonic acids and their derivs. for prophylaxis and treatment of **autoimmune** diseases and **allergies**)
- IT Drug delivery systems
(solns.; medicaments contg. bisphosphonic acids and their derivs. for prophylaxis and treatment of **autoimmune** diseases and **allergies**)
- IT Drug delivery systems
(sprays; medicaments contg. bisphosphonic acids and their derivs. for prophylaxis and treatment of **autoimmune** diseases and **allergies**)
- IT Drug delivery systems
(tablets; medicaments contg. bisphosphonic acids and their derivs. for prophylaxis and treatment of **autoimmune** diseases and **allergies**)
- IT **Immune tolerance**
(to autoantigens and **allergens**, induction of; medicaments contg. bisphosphonic acids and their derivs. for prophylaxis and treatment of **autoimmune** diseases and **allergies**)
- IT Collagens, biological studies
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(type I, autoantigens; medicaments contg. bisphosphonic acids and their derivs. for prophylaxis and treatment of **autoimmune** diseases and **allergies**)
- IT Collagens, biological studies
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(type II, autoantigens; medicaments contg. bisphosphonic acids and their derivs. for prophylaxis and treatment of **autoimmune** diseases and **allergies**)
- IT Collagens, biological studies
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(type III, autoantigens; medicaments contg. bisphosphonic acids and their derivs. for prophylaxis and treatment of **autoimmune** diseases and **allergies**)
- IT **Intestine, disease**
(**ulcerative colitis**; medicaments contg. bisphosphonic acids and their derivs. for prophylaxis and treatment of **autoimmune** diseases and **allergies**)
- IT **Hepatitis**
(**viral, chronic active**; medicaments contg. bisphosphonic acids and their derivs. for prophylaxis and treatment of **autoimmune** diseases and **allergies**)
- IT 11061-68-0, Human insulin
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(autoantigen; medicaments contg. bisphosphonic acids and their derivs. for prophylaxis and treatment of **autoimmune** diseases and **allergies**)
- IT 1984-15-2D, Methanebisphosphonic acid, derivs. 57248-88-1 121268-17-5 138926-19-9
RL: BAC (Biological activity or effector, except adverse); THU (**Therapeutic use**); BIOL (Biological study); USES (Uses)
(medicaments contg. bisphosphonic acids and their derivs. for prophylaxis and treatment of **autoimmune** diseases and **allergies**)
- RE.CNT 1
RE
(1) Anon; EP 594857 A1 HCAPLUS
- IT 1984-15-2D, Methanebisphosphonic acid, derivs.
RL: BAC (Biological activity or effector, except adverse); THU (**Therapeutic use**); BIOL (Biological study); USES (Uses)
(medicaments contg. bisphosphonic acids and their derivs. for

prophylaxis and treatment of **autoimmune** diseases and
allergies)

RN 1984-15-2 HCAPLUS

CN Phosphonic acid, methylenebis- (9CI) (CA INDEX NAME)

H₂O₃P-CH₂-PO₃H₂

L137 ANSWER 3 OF 35 HCAPLUS COPYRIGHT 2001 ACS

AN 1999:565914 HCAPLUS

DN 131:165317

TI Use of a cardiac purinoceptor to effect cellular glucose uptake

IN Liang, Bruce T.; Birnbaum, Morris; Harden, Kendall

PA The Trustees of the University of Pennsylvania, USA

SO PCT Int. Appl., 55 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K031-505

ICS A61K031-52; A61K031-53

CC 1-8 (Pharmacology)

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9943326	A1	19990902	WO 1999-US3881	19990223 <--
	W: AU, CA, JP, US				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9927818	A1	19990915	AU 1999-27818	19990223 <--
PRAI	US 1998-75678		19980224 <--		
	WO 1999-US3881		19990223		
AB	<p>The invention provides a method of detg. whether a compd. is a glucose uptake modulator, including use of a cell comprising an isolated nucleic acid encoding a glucose uptake-enhancing myocardial purinoceptor. The invention also includes (1) a method of enhancing glucose uptake into a mammalian cardiac myocyte by contacting the myocyte and agonists of glucose uptake-enhancing cardiac P2Y2 and P2Y4 purinoceptors, (2) a method of increasing the activity of an intracellular enzyme selected from the group consisting of phospholipase C, protein kinase C, and phosphatidylinositol 3-kinase, and (3) pharmaceutical compns. for use in these methods. The method of enhancing glucose uptake into a cell may be used to minimize ischemic cardiac damage, such as that attributable to angina pectoris, chronic stable angina, unstable angina, post-myocardial infarction angina, myocardial infarction, cardiac arrhythmia, coronary artery disease, diabetes mellitus, and cardiac ischemia attributable to shock, stress, or exertion. ATP was capable of inducing more than a 3-fold enhancement of intracellular inositol phosphate prodn. in cardiac myocytes. This observation was consistent with the presence on the cells of a P2 purinergic receptor, the receptor being capable of stimulating phospholipase C (PLC) activity in cardiac myocytes. Treatment of myocytes with pertussis toxin had no effect on the ability of ATP to enhance inositol phosphate prodn., suggesting that Gq protein is involved in ATP-mediated enhancement of PLC activity. It was obsd. that ATP is capable of increasing the contractile amplitude of the cardiac myocytes. Treating cardiac myocytes with 2-methylthio-ATP, a P2 purinoceptor agonist, caused an increase in contractile amplitude similar to that caused by treating myocytes with ATP. However, 2-methylthio-ATP was not capable of enhancing intracellular PLC activity in myocyte. Furthermore, the increase in contractile amplitude of myocytes mediated by 2-methylthio-ATP was not prevented by treatment with an inhibitor of PLC. Therefore, the P2 receptor which is capable of enhancing intracellular PLC activity appears to be different from the receptor(s) which is capable of enhancing cardiac myocyte contractile amplitude.</p>				
ST	cardioprotectant purinoceptor agonist insulin glucose transport				

- IT Transport proteins
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(GLUT-1 (glucose-transporting, 1), translocation of; cardioprotective compns. contg. agonists of purinoceptor P2Y2 and P2Y4 and insulin, K, or glucose for enhancement of glucose uptake by myocytes in cardiac ischemia).
- IT Transport proteins
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(GLUT-4 (glucose-transporting, 4), translocation of; cardioprotective compns. contg. agonists of purinoceptor P2Y2 and P2Y4 and insulin, K, or glucose for enhancement of glucose uptake by myocytes in cardiac ischemia)
- IT G proteins (guanine nucleotide-binding proteins)
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(Gq; Gq protein in cardioprotection by agonists of purinoceptor P2Y2 and P2Y4)
- IT Purinoceptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(P2U; cardioprotective compns. contg. agonists of purinoceptor P2Y2 and P2Y4 and insulin, K, or glucose for enhancement of glucose uptake by myocytes in cardiac ischemia)
- IT Purinoceptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(P2Y, P2Y4; cardioprotective compns. contg. agonists of purinoceptor P2Y2 and P2Y4 and insulin, K, or glucose for enhancement of glucose uptake by myocytes in cardiac ischemia)
- IT Swine
(Yucatan miniature, myocytes of diabetic minipig; cardioprotective compns. contg. agonists of purinoceptor P2Y2 and P2Y4 and insulin, K, or glucose for enhancement of glucose uptake by myocytes)
- IT Heart, disease
(angina pectoris; cardioprotective compns. contg. agonists of purinoceptor P2Y2 and P2Y4 and insulin, K, or glucose for enhancement of glucose uptake by myocytes in cardiac ischemia)
- IT Heart, disease
(arrhythmia; cardioprotective compns. contg. agonists of purinoceptor P2Y2 and P2Y4 and insulin, K, or glucose for enhancement of glucose uptake by myocytes in cardiac ischemia)
- IT Anti-ischemic agents
Diabetes mellitus
Drug delivery systems
Purinoceptor agonists
(cardioprotective compns. contg. agonists of purinoceptor P2Y2 and P2Y4 and insulin, K, or glucose for enhancement of glucose uptake by myocytes in cardiac ischemia)
- IT Exercise
Shock (circulatory collapse)
Stress, animal
Surgery
(cardioprotective compns. contg. agonists of purinoceptor P2Y2 and P2Y4 and insulin, K, or glucose for enhancement of glucose uptake by myocytes in cardiac ischemia of different origin)
- IT Cytoprotective agents
(cardioprotective; cardioprotective compns. contg. agonists of purinoceptor P2Y2 and P2Y4 and insulin, K, or glucose for enhancement of glucose uptake by myocytes in cardiac ischemia)
- IT Artery, disease
(coronary; cardioprotective compns. contg. agonists of purinoceptor P2Y2 and P2Y4 and insulin, K, or glucose for enhancement of glucose uptake by myocytes in cardiac ischemia)
- IT Muscle
(fiber; cardioprotective compns. contg. agonists of purinoceptor P2Y2 and P2Y4 and insulin, K, or glucose for enhancement of glucose uptake by myocytes)

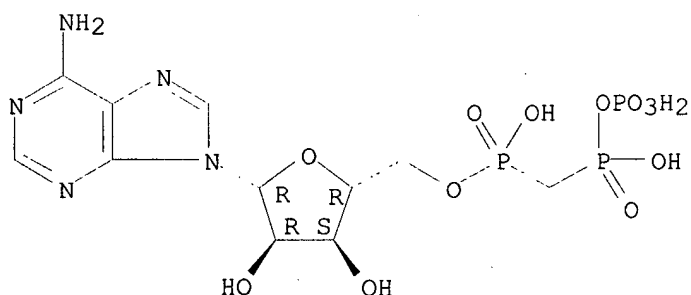
- IT Biological transport
(glucose; cardioprotective compns. contg. agonists of purinoceptor P2Y2 and P2Y4 and insulin, K, or glucose for enhancement of glucose uptake by myocytes in cardiac ischemia)
- IT Heart, disease
(infarction; cardioprotective compns. contg. agonists of purinoceptor P2Y2 and P2Y4 and insulin, K, or glucose for enhancement of glucose uptake by myocytes in cardiac ischemia)
- IT Heart, disease
(ischemia; cardioprotective compns. contg. agonists of purinoceptor P2Y2 and P2Y4 and insulin, K, or glucose for enhancement of glucose uptake by myocytes in cardiac ischemia)
- IT Heart
(myocyte; cardioprotective compns. contg. agonists of purinoceptor P2Y2 and P2Y4 and insulin, K, or glucose for enhancement of glucose uptake by myocytes)
- IT Nucleic acids
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(purinoceptor-encoding; cardioprotective compns. contg. agonists of purinoceptor P2Y2 and P2Y4 and insulin, K, or glucose for enhancement of glucose uptake by myocytes in cardiac ischemia)
- IT Interleukin 1 receptor antagonist
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(translocation of; cardioprotective compns. contg. agonists of purinoceptor P2Y2 and P2Y4 and insulin, K, or glucose for enhancement of glucose uptake by myocytes in cardiac ischemia)
- IT Heart
(ventricle, myocyte; cardioprotective compns. contg. agonists of purinoceptor P2Y2 and P2Y4 and insulin, K, or glucose for enhancement of glucose uptake by myocytes)
- IT 9001-86-9, Phospholipase C 115926-52-8, Phosphatidylinositol 3-kinase 141436-78-4, Protein kinase C
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(activation of; cardioprotective compns. contg. agonists of purinoceptor P2Y2 and P2Y4 and insulin, K, or glucose for enhancement of glucose uptake by myocytes in cardiac ischemia)
- IT 50-99-7, Glucose, biological studies
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(cardioprotective compns. contg. agonists of purinoceptor P2Y2 and P2Y4 and insulin, K, or glucose for enhancement of glucose uptake by myocytes in cardiac ischemia)
- IT 56-65-5, 5'-ATP, biological studies 63-39-8, 5'-UTP 63-39-8D, UTP, analogs 5542-28-9, Diadenosine tetraphosphate 7292-42-4, .alpha.,.beta.-Methylene-adenosine 5'-triphosphate 7440-09-7, Potassium, biological studies 9004-10-8, Insulin, biological studies 35094-46-3, Adenosine 5'-(.gamma.-thio)triphosphate 43170-89-4, 2-Methylthio-adenosine 5'-triphosphate 79049-97-1, Uridine 5'-(.gamma.-thio)triphosphate
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cardioprotective compns. contg. agonists of purinoceptor P2Y2 and P2Y4 and insulin, K, or glucose for enhancement of glucose uptake by myocytes in cardiac ischemia)
- IT 9001-15-4, Creatine kinase
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(cardioprotective compns. contg. agonists of purinoceptor P2Y2 and P2Y4 and insulin, K, or glucose for enhancement of glucose uptake by myocytes in cardiac ischemia)
- IT 50-99-7, D-Glucose, biological studies
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(transport; cardioprotective compns. contg. agonists of purinoceptor P2Y2 and P2Y4 and insulin, K, or glucose for enhancement of glucose uptake by myocytes in cardiac ischemia)

RE.CNT 7

RE

- (1) Liang; US 5712258 A 1998 HCAPLUS
 (2) Liang; US 5859019 A 1999 HCAPLUS
 (3) Scamps; Circ Research 1990, V67, P1007 HCAPLUS
 (4) Tang; Am J Physiol 1996, V270, PE504 HCAPLUS
 (5) Tsuchida; Circ Res 1994, V75(3), P576 HCAPLUS
 (6) Vergauwen; Journal of Clinical Investigation 1994, V93, P974 HCAPLUS
 (7) Williams, M; Ann Rev of Pharmacology and Toxicology 1987, V27, P316
- IT 7292-42-4, .alpha.,.beta.-Methylene-adenosine 5'-triphosphate
 RL: BAC (Biological activity or effector, except adverse); THU
 (Therapeutic use); BIOL (Biological study); USES (Uses)
 (cardioprotective compns. contg. agonists of purinoceptor P2Y2 and P2Y4
 and insulin, K, or glucose for enhancement of glucose uptake by
 myocytes in cardiac ischemia)
- RN 7292-42-4 HCAPLUS
 CN Adenosine, 5'-[hydrogen [[hydroxy(phosphonooxy)phosphinyl)methyl]phosphona
 te] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L137 ANSWER 4 OF 35 HCAPLUS COPYRIGHT 2001 ACS

AN 1999:529179 HCAPLUS

DN 131:169290

TI Treating and diagnosing macrophage-mediated diseases using Fc receptor ligands

IN Van de Winkel, Jan G. J.

PA Medarex, Inc., USA

SO PCT Int. Appl., 77 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM C07K016-28

ICS A61K047-48; G01N033-68

CC 15-3 (Immunochemistry)

Section cross-reference(s): 4

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9941285	A1	19990819	WO 1999-US3488	19990217 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9927721	A1	19990830	AU 1999-27721	19990217 <--
EP 1056781	A1	20001206	EP 1999-908236	19990217 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

NO 2000004098 A 20001002 NO 2000-4098 20000816 <--

PRAI US 1998-74967 19980217 <--

WO 1999-US3488 19990217

AB' The invention provides methods and compns. for selectively targeting macrophages in a localized area. The compns. of the invention include an Fc receptor binding agent, e.g. anti-Fc receptor antibody conjugated to a toxin or a detectable agent. Methods for depleting or inhibiting the activity of macrophages using the compns. of the invention are disclosed. The compns. of the invention can be used therapeutically and diagnostically.

ST antibody Fc receptor toxin label macrophage

IT Ricins

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(A, conjugates; anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)

IT Animal cell line
(ATCC CRL1117; anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)

IT Immunoglobulin receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(IgA; anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)

IT Immunoglobulin receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(IgG type I; anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)

IT Immunoglobulin receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(IgG type II; anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)

IT Immunoglobulin receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(IgG type III; anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)

IT Immunoglobulin receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(IgG; anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)

IT Granulomatous disease
(Wegener's granulomatosis; anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)

IT Animal tissue culture
Colorimetry
Fluorometry
Luminescence spectroscopy
Macrophage
Multiple sclerosis
Psoriasis
Rheumatoid arthritis
(anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)

IT Immunoglobulin receptors
Immunoglobulins

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)

IT Dermatitis
(atopic; anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)

IT Radiochemical analysis
(autoradiog., anal.; anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)

IT Drug delivery systems
(carriers; anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)

- IT Chemistry
(chem. compds., macrophage-binding; anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)
- IT Lung, disease
(chronic obstructive; anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)
- IT Skin, disease
(chronic polymorphic light; anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)
- IT Labels
(conjugate; anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)
- IT Antibodies
Toxins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conjugates; anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)
- IT **Lupus erythematosus**
(cutaneous; anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)
- IT Toxins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(exotoxin A, conjugates; anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)
- IT Human immunodeficiency virus
(infection; anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)
- IT Drug delivery systems
(injections, s.c.; anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)
- IT Encapsulation
(liposome; anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)
- IT Drug delivery systems
(liposomes; anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)
- IT Growth factors, animal
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(macrophage secretion; anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)
- IT Disease, animal
(macrophage-mediated; anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)
- IT Antibodies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(monoclonal, conjugates; anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)
- IT Cell proliferation
(regulator; anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)
- IT Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(saporins, conjugates; anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)
- IT **Connective tissue**
(scleroderma; anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)
- IT Drug delivery systems
(topical; anti-Fc receptor antibody conjugated to toxin or label for diagnosis and treatment of macrophage-mediated diseases)
- IT Drug delivery systems
(transdermal; anti-Fc receptor antibody conjugated to toxin or label

for diagnosis and treatment of macrophage-mediated diseases)

IT 9001-99-4D, Onconase, conjugates 10596-23-3D, derivs.
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (anti-Fc receptor antibody conjugated to toxin or label for diagnosis
 and treatment of macrophage-mediated diseases)

IT 75037-46-6, Gelonin
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (conjugates; anti-Fc receptor antibody conjugated to toxin or label for
 diagnosis and treatment of macrophage-mediated diseases)

RE.CNT 5
 RE
 (1) Fanger, M; US 5635600 A 1997 HCAPLUS
 (2) Kaminski, N; Journal of Immunopharmacology 1986, V8(1), P15 HCAPLUS
 (3) Tempest, P; WO 9410332 A 1994 HCAPLUS
 (4) Univ Pennsylvania; WO 9509002 A 1995 HCAPLUS
 (5) Winkel, J; WO 9809647 A 1998 HCAPLUS

IT 10596-23-3D, derivs.
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (anti-Fc receptor antibody conjugated to toxin or label for diagnosis
 and treatment of macrophage-mediated diseases)

RN 10596-23-3 HCAPLUS
 CN Phosphonic acid, (dichloromethylene)bis- (9CI) (CA INDEX NAME)

H₂O₃P-CCl₂-PO₃H₂

L137 ANSWER 5 OF 35 HCAPLUS COPYRIGHT 2001 ACS
 AN 1999:52239 HCAPLUS
 DN 130:262281
 TI Cyclical etidronate increases bone density in the spine and hip of
 postmenopausal women receiving long term corticosteroid treatment. A
 double blind, randomized placebo controlled study

AU Geusens, Piet; Dequeker, Jan; Vanhoof, Johan; Stalmans, Rita; Boonen,
 Steven; Joly, Jo; Nijs, Jos; Raus, Jef

CS L Willems-Instituut, Limburgs Universitair Centrum, Diepenbeek, B-3590,
 Belg.

SO Ann. Rheum. Dis. (1998), 57(12), 724-727
 CODEN: ARDIAO; ISSN: 0003-4967

PB BMJ Publishing Group
 DT Journal
 LA English
 CC 2-4 (Mammalian Hormones)

AB Objective: To study the effect of cyclic etidronate in secondary
 prevention of corticosteroid induced osteoporosis. Methods: A double
 blind, randomized placebo controlled study comparing cyclic etidronate and
 placebo during two years in 37 postmenopausal women receiving long term
 corticosteroid treatment, mainly for polymyalgia rheumatica (40% of the
 patients) and rheumatoid arthritis (30%). Bone d. was measured in the
 lumbar spine, femoral neck, and femoral trochanter. Results: After two
 years of treatment there was a significant difference between the groups
 in mean per cent change from baseline in bone d. in the spine in favor of
 etidronate (p=0.003). The estd. treatment difference (mean (SD)) was 9.3
 (2.1)%. Etidronate increased bone d. in the spine (4.9 (2.1)%, p<0.05)
 whereas the placebo group lost bone (-2.4 (1.6)%). At the femoral neck
 there was an estd. difference of 5.3 (2.6)% between the groups
 (etidronate: 3.6 (1.4)%, p<0.05, placebo: -2.4 (2.1)%). The estd.
 difference at the trochanter was 8.2 (3.0) (etidronate: 9.0 (1.5)%,
 p<0.0001, placebo: 0.5 (2.3)%). No significant bone loss occurred in the
 hip in placebo treated patients. Conclusion: Cyclic etidronate is an
 effective treatment for postmenopausal women receiving corticosteroid
 treatment and is well tolerated.

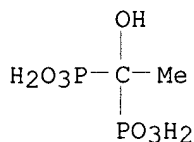
ST cyclical etidronate corticosteroid induced osteoporosis postmenopause;
 rheumatic conditions corticosteroid induced osteoporosis postmenopause
 cyclical etidronate

- IT Antiarthritics
 Antiosteoporotic agents
 Drug toxicity
 Hip
 Postmenopause
Rheumatoid arthritis
 Spine (vertebral column)
 (cyclical etidronate increases bone d. in spine and hip of
 postmenopausal women receiving long term corticosteroid treatment for
 rheumatic conditions)
- IT Corticosteroids, biological studies
 RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (cyclical etidronate increases bone d. in spine and hip of
 postmenopausal women receiving long term corticosteroid treatment for
 rheumatic conditions)
- IT Muscle diseases
 (polymyalgia rheumatica; cyclical etidronate increases bone d. in spine
 and hip of postmenopausal women receiving long term corticosteroid
 treatment for rheumatic conditions)
- IT 50-24-8, Prednisolone
 RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (cyclical etidronate increases bone d. in spine and hip of
 postmenopausal women receiving long term corticosteroid treatment for
 rheumatic conditions)
- IT **2809-21-4**
 RL: BAC (Biological activity or effector, except adverse); THU
(Therapeutic use); BIOL (Biological study); USES (Uses)
 (cyclical etidronate increases bone d. in spine and hip of
 postmenopausal women receiving long term corticosteroid treatment for
 rheumatic conditions)

RE.CNT 27

- RE
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 - (2) Adachi, J; J Rheumatol 1996, V23, P995 HCAPLUS
 - (3) Adachi, J; N Engl J Med 1997, V337, P382 HCAPLUS
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 - (16) Hooyman, J; Arthritis Rheum 1984, V27, P1353 MEDLINE
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 - (25) Struys, A; Am J Med 1994, V99, P235
 - (26) Verhoeven, A; J Rheumatol 1997, V24, P1495 HCAPLUS
 - (27) Walsch, L; BMJ 1996, V313, P344
- IT **2809-21-4**
 RL: BAC (Biological activity or effector, except adverse); THU
(Therapeutic use); BIOL (Biological study); USES (Uses)
 (cyclical etidronate increases bone d. in spine and hip of
 postmenopausal women receiving long term corticosteroid treatment for

rheumatic conditions)
 RN 2809-21-4 HCAPLUS
 CN Phosphonic acid, (1-hydroxyethylidene)bis- (9CI) (CA INDEX NAME)



L137 ANSWER 6 OF 35 HCAPLUS COPYRIGHT 2001 ACS

AN 1999:27846 HCAPLUS

DN 130:66812

TI Tartrate salt of a substituted dipeptide as growth hormone secretagogue

IN Carpino, Philip Albert; Dasilva-Jardine, Paul Andrew; Lefker, Bruce Allen; Murry, Jerry Anthony

PA Pfizer Products Inc., USA

SO PCT Int. Appl., 50 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM C07K005-023

ICS A61K038-06; C07D401-06; C07D471-04; C07D471-04; C07D231-00; C07D221-00

CC 34-3 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 1, 2, 63

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9858948	A1	19981230	WO 1998-IB874	19980605 <--
	W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
	AU 9874455	A1	19990104	AU 1998-74455	19980605 <--
	EP 989993	A1	20000405	EP 1998-921681	19980605 <--
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO			
	BR 9810623	A	20000725	BR 1998-10623	19980605 <--
	JP 2000514840	T2	20001107	JP 1999-504027	19980605 <--
	NO 9906469	A	20000223	NO 1999-6469	19991223 <--
PRAI	US 1997-50723		19970625 <--		
	WO 1998-IB874		19980605 <--		
OS	MARPAT 130:66812				
AB	Growth hormone secretagogue 2-amino-N-{1-(2,4-difluorobenzyloxymethyl)-2-oxo-2-[3-oxo-3a-pyridin-2-ylmethyl-2-(2,2,2-trifluoroethyl)-2,3,3a,4,6,7-hexahydropyrazolo[4,3-c]pyridin-5-yl]ethyl}-2-methylpropionamide L-tartrate was prepd. The synthesis involved reactions of 4-oxopiperidine-1,3-dicarboxylic acid 1-tert-Bu, 3-Et ester, picolyl chloride hydrochloride, CF3CH2NHNH2, N-Boc-D-serine, 2,4-difluorobenzyl bromide, 2-tert-butoxycarbonylamino-2-methylpropionic acid 2,5-dioxopyrrolidin-1-yl ester, and tartaric acid.				
ST	dipeptide tartrate prepn growth hormone secretagogue				
IT	Adrenoceptor agonists				
	Aging (animal)				
	Heart failure				
	Hyperglycemia				
	Insulin dependent diabetes mellitus				
	Non-insulin-dependent diabetes mellitus				

Obesity
 Osteoporosis
 Sleep disorders
 (prepn. of substituted dipeptide tartrate as growth hormone
 secretagogue)

IT Peptides, preparation
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
 (prepn. of substituted dipeptide tartrate as growth hormone
 secretagogue)

IT Conjugated estrogens
 Estrogens
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (prepn. of substituted dipeptide tartrate as growth hormone
 secretagogue)

IT 5042-30-8, 2,2,2-Trifluoroethylhydrazine 6368-20-3 6959-47-3, Picolyl
 chloride hydrochloride 23915-07-3, 2,4-Difluorobenzyl bromide
 98977-34-5 104055-39-2
 RL: RCT (Reactant)
 (prepn. of substituted dipeptide tartrate as growth hormone
 secretagogue)

IT 193272-70-7P 218163-73-6P 218163-74-7P 218163-76-9P 218163-78-1P
 218163-79-2P 218163-81-6P 218163-82-7P 218163-83-8P 218163-91-8P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
 (prepn. of substituted dipeptide tartrate as growth hormone
 secretagogue)

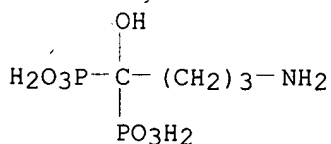
IT 218163-71-4P 218163-84-9P 218163-87-2P 218163-89-4P
 RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
 study); PREP (Preparation); USES (Uses)
 (prepn. of substituted dipeptide tartrate as growth hormone
 secretagogue)

IT 57-83-0, Progesterone, biological studies 9007-12-9, Calcitonin
 10540-29-1, Tamoxifen **66376-36-1**, Alendronate 82413-20-5,
 Droloxifene 84449-90-1, Raloxifene **114084-78-5**, Ibandronate
 116057-75-1, Idoxifene 180915-78-0 180915-84-8 180915-86-0
 180916-14-7 180916-15-8 180916-16-9 193274-89-4
 RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
 (prepn. of substituted dipeptide tartrate as growth hormone
 secretagogue)

RE.CNT 3
 RE
 (1) Merck & Co Inc; WO 9413696 A 1994 HCAPLUS
 (2) Morriello, G; WO 9513069 A 1995 HCAPLUS
 (3) Pfizer; WO 9724369 A 1997 HCAPLUS

IT **66376-36-1**, Alendronate
 RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
 (prepn. of substituted dipeptide tartrate as growth hormone
 secretagogue)

RN 66376-36-1 HCAPLUS
 CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)



L137 ANSWER 7 OF 35 HCAPLUS COPYRIGHT 2001 ACS
 AN 1998:731646 HCAPLUS
 DN 130:133755
 TI Skin reactions associated with bisphosphonates: a report of 3 cases and an
 approach to management
 AU Phillips, Elizabeth; Knowles, Sandra; Weber, Elizabeth; Shear, Neil H.
 CS Departments of Medicine (Clinical Pharmacology, Sunnybrook Health Science

Centre, Toronto, ON, Can.
 SO J. Allergy Clin. Immunol. (1998), 102(4, Pt. 1), 697-698
 CODEN: JACIBY; ISSN: 0091-6749
 PB Mosby, Inc.
 DT Journal
 LA English
 CC 1-6 (Pharmacology)
 AB The cutaneous reactions assocd. with bisphosphonate therapy in patients with breast cancer and the management of these reactions were reported in 3 cases. The cutaneous reactions to clodronate and pamidronate appear to be IgE-mediated and include urticaria, angioedema, hypotension, and (or) tachycardia occurring within 48 h after initiation of treatment. Oral challenge and desensitization with alendronate, a bisphosphonate structurally similar to pamidronate, allowed 2 of the patients to continue using this class of medication. The usefulness of skin testing for bisphosphonate reactions need to be validated, since the haptens that may be involved in IgE-mediated reactions to these drugs are unknown, as is the predictive value of the parent compds. as skin-testing material.
 ST clodronate pamidronate alendronate etidronate bisphosphonate anticancer
 IT **Allergies**
 Breast tumor inhibitors
 (skin reactions assocd. with bisphosphonate treatment in breast cancer patients)
 IT IgE
 RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BIOL (Biological study)
 (skin reactions assocd. with bisphosphonate treatment in breast cancer patients)
 IT 10596-23-3 40391-99-9 66376-36-1, Alendronate
 RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
 (skin reactions assocd. with bisphosphonate treatment in breast cancer patients)
 IT 2809-21-4 13598-36-2D, Phosphonic acid, alkylidenebis- derivs.
 RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
 (skin reactions assocd. with bisphosphonate treatment in breast cancer patients)
 RE.CNT 6
 RE
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 (3) Mautalen, C; Br Med J 1984, V288, P828 MEDLINE
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 (5) Pajus, I; Br Med J 1993, V307, P484 MEDLINE
 (6) Roux, C; Calcif Tissue Int 1992, V50, P78
 IT 10596-23-3
 RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
 (skin reactions assocd. with bisphosphonate treatment in breast cancer patients)
 RN 10596-23-3 HCAPLUS
 CN Phosphonic acid, (dichloromethylene)bis- (9CI) (CA INDEX NAME)

H₂O₃P-CCl₂-PO₃H₂

L137 ANSWER 8 OF 35 HCAPLUS COPYRIGHT 2001 ACS
 AN 1998:706502 HCAPLUS
 DN 130:90420
 TI Liposome-encapsulated Clodronate retards the development of experimental

autoimmune uveitis

AU Niesman, Michael R.; Ni, Ming; Bloom, Jeffrey N.
 CS Agouron Pharmaceuticals, San Diego, CA, 92121, USA
 SO J. Liposome Res. (1998), 8(3), 367-379
 CODEN: JLREE7; ISSN: 0898-2104
 PB Marcel Dekker, Inc.
 DT Journal
 LA English
 CC 1-11 (Pharmacology)
 Section cross-reference(s): 14, 15, 63

AB A study was undertaken to det. if the i.v. injection of liposome-encapsulated dichloromethylene diphosphonate (Cl2MDP; Clodronate), a treatment known to deplete monocytes, as well as liver and spleen macrophages, would reduce the no. of macrophages in the retina of animals with exptl. **autoimmune uveitis** (EAU) and decrease the severity of the disease. EAU was induced in Lewis rats by immunization with S-antigen (S-Ag). Monocytes and macrophages were depleted via an i.v. injection of Cl2MDP encapsulated in liposomes. Control groups included rats that received no S-Ag (n=18), S-Ag and no treatment (n=23), S-Ag and free drug (n=20), or empty liposomes (n=14). Treated animals received injections of the Cl2MDP-liposomes, free drug, or empty liposomes. Animals were sacrificed at 14, 21 and 28 days post-S-Ag administration. I.v., Cl2MDP-liposomes produced a statistically significant redn. in the severity of the EAU when compared to controls at both days 14 and 21 following S-Ag injection. Immunohistochem. staining with the monoclonal antibody ED1 demonstrated that the severity of the ocular inflammatory response correlated with the no. of ED1-pos. cells in the retina. Following the cessation of treatment, treated animals developed disease that was as severe at day 28 as that of untreated animals at day 21. These results confirm the importance of monocytes and macrophages in EAU by demonstrating the correlation between the presence of ED1-pos. cells in the retina and the resultant damage to the retina. Although the dosing regimen employed here did not provide a cure, strategies designed to prevent the local recruitment and/or activation of mononuclear phagocytes may prove to be useful in the treatment of EAU.

ST Clodronate liposome **autoimmune uveitis** treatment
 IT **Uveitis**
 (autoimmune; liposome-encapsulated Clodronate retards the development of exptl. **autoimmune uveitis** by depletion of monocytes and macrophages)

IT Liposomes (drug delivery systems)
 Macrophage
 Monocyte
 (liposome-encapsulated Clodronate retards the development of exptl. **autoimmune uveitis** by depletion of monocytes and macrophages)

IT **Autoimmune diseases**
 (uveitis; liposome-encapsulated Clodronate retards the development of exptl. **autoimmune uveitis** by depletion of monocytes and macrophages)

IT 10596-23-3
 RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (liposome-encapsulated Clodronate retards the development of exptl. **autoimmune uveitis** by depletion of monocytes and macrophages)

RE.CNT 30
 RE
 (1) Bautista, A; J Leukoc Biol 1994, V55, P321 HCAPLUS
 (2) Berra, A; Invest Ophthalmol Vis Sci 1994, V35, P2990 MEDLINE
 (3) Caspi, R; J Immunol 1986, V136, P928 MEDLINE
 (4) Claassen, E; J Microencaps 1986, V3, P109 HCAPLUS
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- (20) McMenamin, P; Micron 1993, V24, P521
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- (25) Shinohara, T; Progress in Retinal Research 1988, P51 HCAPLUS
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- (29) van Rooijen, N; J Immuno Meth 1989, V124, P1 HCAPLUS
- (30) Vidal, M; Embo J 1985, V4, P2461 HCAPLUS

IT 10596-23-3

RL: BAC (Biological activity or effector, except adverse); THU
(Therapeutic use); BIOL (Biological study); USES (Uses)

(liposome-encapsulated Clodronate retards the development of exptl.
autoimmune uveitis by depletion of monocytes and
macrophages)

RN 10596-23-3 HCAPLUS

CN Phosphonic acid, (dichloromethylene)bis- (9CI) (CA INDEX NAME)

H₂O₃P-CCl₂-PO₃H₂

L137 ANSWER 9 OF 35 HCAPLUS COPYRIGHT 2001 ACS

AN 1998:574148 HCAPLUS

DN 129:339833

TI Effects of alendronate sodium on severe osteodystrophy in postmenopausal
patients with **primary biliary cirrhosis**: a
pilot study

AU Floreani, Annarosa; Tizian, Luisa; Luisetto, Giovanni; Buda, Andrea; Mega,
Andrea; Naccarato, Remo

CS Department of Gastroenterology, University of Padova, Padua, 35100, Italy

SO Curr. Ther. Res. (1998), 59(8), 589-593

CODEN: CTCEA9; ISSN: 0011-393X

PB Excerpta Medica

DT Journal

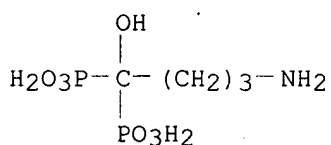
LA English

CC 1-12 (Pharmacology)

AB Osteodystrophy is a major complication in **primary biliary cirrhosis** (PBC) and a significant problem for patients who require a liver transplant. Treatment for osteodystrophy has yet to be standardized. The goal of this pilot study was to assess the efficacy and tolerability of alendronate sodium, a potent specific inhibitor of osteoclast-mediated bone resorption. The study comprised 15 postmenopausal PBC patients (mean age, 64.25 +/- 8.77 yr) with severe osteodystrophy. Four patients had histol. stage II disease, 8 stage III, and 3 stage IV. All patients had a T score below 2, indicating a fracture risk of 60%. All patients received two courses of alendronate sodium (10 mg/d for 3 mo, sepd. by a 2-mo interval). The following variables were assessed at baseline and after 10 mo: bone mineral d. (BMD) (by dual-energy x-ray absorptiometry in the lumbar spine), calcium, sodium, potassium, creatinine, 25-hydroxyvitamin D, parathyroid hormone, and osteocalcin. No patients dropped out of the study, and therapy was well

tolerated by all patients. At the end of treatment, BMD increased significantly compared with baseline (0.714 \pm 0.115 g/cm² vs 0.740 \pm 0.108 g/cm²). Although not statistically significant, a trend toward an increase in serum osteocalcin levels (1.4 \pm 1.5 ng/mL vs 2.6 \pm 1.4 ng/mL) was evident. These preliminary findings suggest that alendronate sodium may be helpful in treating severe osteodystrophy in postmenopausal patients with PBC. Larger, controlled trials using long-term treatment with alendronate sodium are needed to establish the efficacy and safety of this drug.

- ST alendronate sodium osteodystrophy postmenopause
 IT Postmenopause
 (effects of alendronate sodium on severe osteodystrophy in postmenopausal humans with **primary biliary cirrhosis**)
 IT Bone diseases
 (osteodystrophy, inhibitors; effects of alendronate sodium on severe osteodystrophy in postmenopausal humans with **primary biliary cirrhosis**)
 IT **129318-43-0**, Alendronate sodium
 RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
 (effects of alendronate sodium on severe osteodystrophy in postmenopausal humans with **primary biliary cirrhosis**)
 IT **129318-43-0**, Alendronate sodium
 RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
 (effects of alendronate sodium on severe osteodystrophy in postmenopausal humans with **primary biliary cirrhosis**)
 RN **129318-43-0** HCAPLUS
 CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, monosodium salt (9CI) (CA INDEX NAME)



● Na

L137 ANSWER 10 OF 35 HCAPLUS COPYRIGHT 2001 ACS

AN 1998:542529 HCAPLUS

DN 129:254608

TI Effect of combined cyclosporine A and liposome encapsulated dichloromethylene diphosphonate on the organization of the rat thymus: evidence for a role of macrophages in guiding the post cyclosporine A thymic reorganization

AU Rezzani, R.; Rodella, L.; Bianchi, R.

CS Department of Biomedical Sciences and Biotechnology, Division of Human Anatomy, University of Brescia, Brescia, 19-25123, Italy

SO Int. J. Immunopharmacol. (1998), 20(4/5), 183-192

CODEN: IJIMDS; ISSN: 0192-0561

PB Elsevier Science Ltd.

DT Journal

LA English

CC 1-7 (Pharmacology)

Section cross-reference(s): 15

AB Cyclosporine A (CsA) is a powerful immunosuppressant inducing marked involution of the thymic medulla, and disappearance of interdigitating cells (IDCs) and reducing the no. of macrophages (M.phi.). Usually, while the thymus of rats receiving a short course of CsA promptly recovers after stopping CsA treatment, long term CsA treatment, like mediastinal irradiation, impairs the normal thymic recovery and is thought to be responsible for the development of **autoimmune** diseases. In the present study we evaluated the role played by the IDCs and M.phi. in the normal recovery of the thymic histology at light and ultrastructural level. Besides CsA administration, we also used liposome-encapsulated dichloromethylenediphosphonate (lip-CL2MDP), that induces a total depletion of the M.phi. resistant to CsA. After a short (21 days) course of CsA and lip-CL2MDP administration, we did not observe the normal recovery of the thymic parenchyma but only cortical zones consisting of lymphoblasts, epithelial cells and M.phi.. The CsA/lip-CL2MDP treatment detouring the loss of IDCs and M.phi. and consequently the loss of the normal thymic histology seems to simulate in the rats, the long term CsA treatment or the mediastinal irradiation. The results obtained suggest that the loss of IDCs and the depletion of M.phi. interfere with the normal thymic recovery. The delay in the recovery of IDCs could be a consequence of the absence of macrophages. These findings would indicate that the IDCs, detouring the negative selection of T-lymphocytes, are the main cells responsible for the thymic microenvironment.

ST cyclosporine thymus reorganization macrophage

IT **Autoimmune diseases**
Langerhans' cell
Liposomes (drug delivery systems)
Macrophage
Thymus gland
(role of macrophages in guiding post cyclosporine A thymic reorganization)

IT 59865-13-3, Cyclosporine A
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(role of macrophages in guiding post cyclosporine A thymic reorganization)

IT 10596-23-3
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(role of macrophages in guiding post cyclosporine A thymic reorganization)

IT 10596-23-3
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(role of macrophages in guiding post cyclosporine A thymic reorganization)

RN 10596-23-3 HCAPLUS

CN Phosphonic acid, (dichloromethylene)bis- (9CI) (CA INDEX NAME)

H₂O₃P-CCl₂-PO₃H₂

L137 ANSWER 11 OF 35 HCAPLUS COPYRIGHT 2001 ACS

AN 1998:62552 HCAPLUS

DN 128:119687

TI Topical compositions containing chelators for **allergic** dermatitis

IN Ito, Masatoshi; Fujii, Masashi

PA Fujii, Masashi, Japan

SO Jpn. Kokai Tokkyo Koho, 9 pp.
CODEN: JKXXAF

DT Patent

LA Japanese

IC ICM A61K045-00

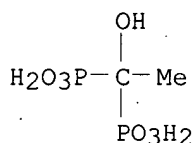
ICS A61K031-195; A61K031-66; A61K033-42; C09K003-00

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 1

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 10017493	A2	19980120	JP 1996-207532	19960702 <--
AB	Topical compns. for treatment of allergic dermatitis contain ion chelators for calcium are claimed. An ointment contained menthol 0.1, EDTA 0.1 and white petrolatum to 100 wt.%. ST topical pharmaceutical chelator allergic dermatitis				
IT	Allergic dermatitis Chelating agents Ointments (drug delivery systems) Topical drug delivery systems (topical compns. contg. chelators for treatment of allergic dermatitis)				
IT	60-00-4, EDTA, biological studies 83-86-3, Phytic acid 2809-21-4, Hydroxyethanediphosphonic acid RL: THU (Therapeutic use) ; BIOL (Biological study); USES (Uses) (topical compns. contg. chelators for treatment of allergic dermatitis)				
IT	2809-21-4, Hydroxyethanediphosphonic acid RL: THU (Therapeutic use) ; BIOL (Biological study); USES (Uses) (topical compns. contg. chelators for treatment of allergic dermatitis)				
RN	2809-21-4 HCAPLUS				
CN	Phosphonic acid, (1-hydroxyethylidene)bis- (9CI) (CA INDEX NAME)				



L137 ANSWER 12 OF 35 HCAPLUS COPYRIGHT 2001 ACS

AN 1997:772117 HCAPLUS

DN 128:97459

TI The effect of TRK-530 on experimental arthritis in mice

AU Takaoka, Yuko; Nagai, Hiroichi; Mori, Hiroshi; Tanahashi, Masahiko

CS Department of Pharmacology, Gifu Pharmaceutical University, Gifu, 502, Japan

SO Biol. Pharm. Bull. (1997), 20(11), 1147-1150

CODEN: BPBLEO; ISSN: 0918-6158

PB Pharmaceutical Society of Japan

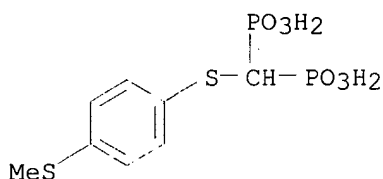
DT Journal

LA English

CC 1-7 (Pharmacology)

AB TRK-530 is a newly synthesized diphosphonate deriv. We investigated the effect of TRK-530 on type II collagen-induced arthritis (CIA) in mice in comparison to that of prednisolone and indomethacin. TRK-530 at a dose of 25 mg/kg showed a tendency to inhibit CIA. TRK-530 at a dose of 50 mg/kg inhibited the development of the CIA in terms of the progression of footpad swelling, bone damage and histopathol. changes. TRK-530 at a dose of 50 mg/kg also significantly inhibited the delayed type hypersensitivity (DTH) response to type II collagen, but not the prodn. of anti-type II collagen IgG antibody in arthritic mice. To investigate the inhibitory mechanism of TRK-530, the type of effect of TRK-530 on the prodn. of IL-1.β. in vitro was studied. TRK-530 at a concn. of 10⁻⁴ M inhibited LPS-induced IL-1.β. prodn. from J774.1 cells. In conclusion, TRK-530 inhibited CIA in mice. The inhibition of the DTH reaction to type II collagen and the inhibition of IL-1.β. prodn. may partly participate the anti-rheumatoid action of TRK-530.

ST diphosphonate TRK530 antiarthritic antirheumatic interleukin
 IT Antiarthritics
 Antirheumatic drugs
 (effect of diphosphonate deriv. TRK-530 on exptl. arthritis in mice)
 IT **Delayed hypersensitivity**
 (inhibition of; effect of diphosphonate deriv. TRK-530 on exptl.
 arthritis in mice)
 IT Interleukin 1.beta..
 RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
 (inhibition of; effect of diphosphonate deriv. TRK-530 on exptl.
 arthritis in mice)
 IT **151425-92-2, TRK 530**
 RL: BAC (Biological activity or effector, except adverse); **THU**
(Therapeutic use); BIOL (Biological study); USES (Uses)
 (effect of diphosphonate deriv. TRK-530 on exptl. arthritis in mice)
 IT **151425-92-2, TRK 530**
 RL: BAC (Biological activity or effector, except adverse); **THU**
(Therapeutic use); BIOL (Biological study); USES (Uses)
 (effect of diphosphonate deriv. TRK-530 on exptl. arthritis in mice)
 RN 151425-92-2 HCAPLUS
 CN Phosphonic acid, [[[4-(methylthio)phenyl]thio]methylene]bis-, disodium
 salt (9CI) (CA INDEX NAME)



● 2 Na

L137 ANSWER 13 OF 35 HCAPLUS COPYRIGHT 2001 ACS
 AN 1997:757141 HCAPLUS
 DN 128:30414
 TI Isopentenyl pyrophosphate isomerase and/or prenyl transferase inhibitors
 for therapeutic use
 IN Brown, Richard John; Watts, Donald Jeremy; Russel, Robert Graham Goodwin;
 Rogers, Michael John
 PA University of Sheffield, UK; Brown, Richard John; Watts, Donald Jeremy;
 Russel, Robert Graham Goodwin; Rogers, Michael John
 SO PCT Int. Appl., 76 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 IC ICM C12Q
 CC 1-12 (Pharmacology)
 Section cross-reference(s): 5

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9743437	A2	19971120	WO 1997-GB1302	19970512 <--
	WO 9743437	A3	19980226		
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW:	GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN,				

ML, MR, NE, SN, TD, TG

AU 9727833 A1 19971205 AU 1997-27833 19970512 <--

EP 952834 A2 19991103 EP 1997-921954 19970512 <--

R: AT, BE, CH, DE, ES, FR, GB, IT, LI, NL, SE, IE

PRAI GB 1996-10174 19960515 <--

GB 1997-8329 19970425 <--

WO 1997-GB1302 19970512 <--

AB Prenyl transferase (farnesyl pyrophosphate synthase) and/or isopentenyl pyrophosphate isomerase inhibitors find application in various forms of therapy and prophylaxis. The use of such inhibitors in the treatment of various diseases and disorders of bone metab.; in the screening, isolation, synthesis and the evaluation of osteoactive drugs; and as hypolipidemic and anti-cancer agents is also described. Herbicides and fungicides comprising prenyl transferase and/or isopentenyl pyrophosphate isomerase inhibitors are also disclosed.

ST isopentenyl pyrophosphate isomerase inhibitor therapeutic; prenyl transferase inhibitor therapeutic; bone metab disorder hypolipidemic anticancer therapeutic; herbicide fungicide prenyl transferase inhibitor; fungicide herbicide isopentenyl pyrophosphate isomerase inhibitor

IT Proteins (specific proteins and subclasses)

RL: BPR (Biological process); BIOL (Biological study); PROC (Process) (CaaX box-contg., prenylation; isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)

IT Proteins (specific proteins and subclasses)

RL: BPR (Biological process); BIOL (Biological study); PROC (Process) (Rab6; isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)

IT Arterial restenosis

(after coronary angioplasty; isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)

IT Familial hypercholesterolemia

(and homozygous familial hypercholesterolemia; isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)

IT Coronary artery

(angioplasty, restenosis after; isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)

IT Isoprenoids

RL: BPR (Biological process); BIOL (Biological study); PROC (Process) (apoptosis related to; isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)

IT Bone tumors

Metastasis inhibitors

(bone metastasis inhibitors; isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)

IT Antitumor agents

Metabolism

(bone; isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)

IT Carboxylic acids, biological studies

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (carboxylates and phosphonocarboxylates; isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)

IT High-density lipoproteins

Low-density lipoproteins

RL: BPR (Biological process); BIOL (Biological study); PROC (Process) (cholesterol; isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)

IT Angioplasty

(coronary, restenosis after; isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)

IT Liver

(dysfunction, lipid metab. modulation in; isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for

therapeutic use)

IT Drug screening
(for osteoactive drugs; isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)

IT Proteins (general), biological studies
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(hyperproteinemia; isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)

IT Dipeptides
RL: BAC (Biological activity or effector, except adverse); THU
(Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitor conjugates; isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)

IT Bone tumors
(inhibitors; isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)

IT Dictyostelium
Dictyostelium discoideum
(isopentenyl pyrophosphate isomerase and prenyl transferase; isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)

IT Allograft
Anti-inflammatory drugs
Antiarthritics
Antiatherosclerotics
Anticholesteremic agents
Antiosteoporotic agents
Antiproliferative agents
Antitumor agents
Apoptosis
Autoimmune diseases
~~Bladder carcinoma inhibitors~~
Bone resorption inhibitors
Brain tumor inhibitors
Cardiovascular agents
Cell proliferation
Colon tumor inhibitors
Diagnostic agents
Drug design
Farnesylation
Fungicides
Herbicides
Hypercalcemia
Hyperlipoproteinemia
Hypolipemic agents
Imaging agents
Lipid metabolic diseases
Lung tumor inhibitors
Molecular modeling
Paget's disease of bone
Prenylation
Signal transduction (biological)
Test kits
Transplant rejection
(isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)

IT Diphosphates
RL: BAC (Biological activity or effector, except adverse); THU
(Therapeutic use); BIOL (Biological study); USES (Uses)
(isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)

IT Glycerides, biological studies
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)

IT LDL receptors

- RL: BSU (Biological study, unclassified); BIOL (Biological study)
(isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)
- IT Arterial diseases
(lesion; isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)
- IT Macrophage
(mevastatin effect on macrophage apoptosis)
- IT Hyperlipidemia
(nephrotic; isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)
- IT Bone
(osteoactive bisphosphonates; isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)
- IT Drugs
(osteoactive; isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)
- IT Proteins (general), biological studies
Ras proteins
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(prenylation; isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)
- IT Sulfonic acids, biological studies
RL: BAC (Biological activity or effector, except adverse); THU
(Therapeutic use); BIOL (Biological study); USES (Uses)
(sulfonates; isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)
- IT Alkenylation
(tetramethylhexadecatetraenylation; isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)
- IT Antibodies
Monoclonal antibodies
RL: BAC (Biological activity or effector, except adverse); THU
(Therapeutic use); BIOL (Biological study); USES (Uses)
(to isopentenyl pyrophosphate isomerase or prenyl transferase; isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)
- IT 9032-79-5, Prenyl transferase 9033-27-6, Isopentenyl pyrophosphate isomerase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)
- IT 10596-23-3 13598-36-2D, Phosphonic acid, bisphosphonates
40391-99-9 40391-99-9D, analogs and derivs.
66376-36-1, Alendronate 66376-36-1D, Alendronate, analogs and derivs. 105462-24-6 114084-78-5, Ibandronate 114084-78-5D, Ibandronate, analogs and derivs. 138330-18-4, YM175 199668-51-4D, analogs
RL: BAC (Biological activity or effector, except adverse); THU
(Therapeutic use); BIOL (Biological study); USES (Uses)
(isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)
- IT 57-88-5, Cholesterol, biological studies
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)
- IT 674-26-0, Mevalonic acid lactone 6699-20-3, Geranylgeranyl pyrophosphate 13058-04-3, Farnesyl pyrophosphate 73573-88-3, Mevastatin
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(mevastatin effect on macrophage apoptosis)
- IT 10596-23-3
RL: BAC (Biological activity or effector, except adverse); THU
(Therapeutic use); BIOL (Biological study); USES (Uses)
(isopentenyl pyrophosphate isomerase inhibitors and/or prenyl transferase inhibitors for therapeutic use)

RN 10596-23-3 HCAPLUS
 CN Phosphonic acid, (dichloromethylene)bis- (9CI) (CA INDEX NAME)

H₂O₃P-CCl₂-PO₃H₂

L137 ANSWER 14 OF 35 HCAPLUS COPYRIGHT 2001 ACS

AN 1997:735846 HCAPLUS

DN 127:341814

TI Uses of inorganic pyrophosphates in treatment of diseases related to inappropriate or inadequate ABC protein activity

IN Welsh, Michael J.

PA University of Iowa Research Foundation, USA

SO U.S., 15 pp.

CODEN: USXXAM

DT Patent

LA English

IC ICM A61K033-42

NCL 424601000

CC 1-12 (Pharmacology)

Section cross-reference(s): 63

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5686114	A	19971111	US 1995-484847	19950602 <--
	US 5958907	A	19990928	US 1997-920999	19970829 <--
PRAI	US 1995-484847		19950602		<--
AB	Pharmaceutical compns. are disclosed which comprise an inorg. pyrophosphate (PPI) in a form that renders the PPI accessible to ABC proteins when administered to a subject in vivo; also disclosed are use of the compns. for treating subjects having a disease or disorder assocd. with inappropriate or inadequate ABC protein activity (e.g., cystic fibrosis, multidrug resistance, Zellweger's Syndrome).				
ST	inorg pyrophosphate pharmaceutical ABC protein disease				
IT	CFTR (cystic fibrosis transmembrane conductance regulator)				
	RL: BPR (Biological process); BIOL (Biological study); PROC (Process) (508-dephenylalanine-; inorg. pyrophosphates in treatment of diseases related to inappropriate or inadequate ABC protein activity)				
IT	Proteins (specific proteins and subclasses)				
	RL: BPR (Biological process); BIOL (Biological study); PROC (Process) (ABC (ATP-binding cassette-contg.); inorg. pyrophosphates in treatment of diseases related to inappropriate or inadequate ABC protein activity)				
IT	Diseases (animal)				
	(ABC protein-related; inorg. pyrophosphates in treatment of diseases related to inappropriate or inadequate ABC protein activity)				
IT	Mutation				
	(CFTR; inorg. pyrophosphates in treatment of diseases related to inappropriate or inadequate ABC protein activity)				
IT	Proteins (specific proteins and subclasses)				
	RL: BPR (Biological process); BIOL (Biological study); PROC (Process) (PMP70; inorg. pyrophosphates in treatment of diseases related to inappropriate or inadequate ABC protein activity)				
IT	Lipidosis				
	Nervous system diseases				
	(Refsum disease, infantile; inorg. pyrophosphates in treatment of diseases related to inappropriate or inadequate ABC protein activity)				
IT	Proteins (specific proteins and subclasses)				
	RL: BPR (Biological process); BIOL (Biological study); PROC (Process) (TAP (transporter in antigen processing); inorg. pyrophosphates in treatment of diseases related to inappropriate or inadequate ABC protein activity)				
IT	MHC antigens				
	RL: BSU (Biological study, unclassified); BIOL (Biological study)				

(TAP-mediated antigen presentation linked to; inorg. pyrophosphates in treatment of diseases related to inappropriate or inadequate ABC protein activity)

IT Antigen presentation
(TAP-mediated; inorg. pyrophosphates in treatment of diseases related to inappropriate or inadequate ABC protein activity)

IT Epithelium
(apical membrane; inorg. pyrophosphates in treatment of diseases related to inappropriate or inadequate ABC protein activity)

IT Drug resistance
(chemotherapeutic; inorg. pyrophosphates in treatment of diseases related to inappropriate or inadequate ABC protein activity)

IT Apical membrane
(epithelial; inorg. pyrophosphates in treatment of diseases related to inappropriate or inadequate ABC protein activity)

IT **Autoimmune diseases**
Constipation
Cystic fibrosis
Drug delivery systems
Laxatives
Transplant rejection
Zellweger syndrome
(inorg. pyrophosphates in treatment of diseases related to inappropriate or inadequate ABC protein activity)

IT CFTR (cystic fibrosis transmembrane conductance regulator)
P-glycoproteins
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(inorg. pyrophosphates in treatment of diseases related to inappropriate or inadequate ABC protein activity)

IT Biological simulation
(kinetic; inorg. pyrophosphates in treatment of diseases related to inappropriate or inadequate ABC protein activity)

IT Brain diseases
(neonatal adrenoleukodystrophy; inorg. pyrophosphates in treatment of diseases related to inappropriate or inadequate ABC protein activity)

IT Chemotherapy
(resistance; inorg. pyrophosphates in treatment of diseases related to inappropriate or inadequate ABC protein activity)

IT 535-75-1, Pipecolic acid
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(hyperpipecolic acidemia; inorg. pyrophosphates in treatment of diseases related to inappropriate or inadequate ABC protein activity)

IT 142008-29-5, CAMP-dependent protein kinase
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BIOL (Biological study); PROC (Process)
(inorg. pyrophosphates in treatment of diseases related to inappropriate or inadequate ABC protein activity)

IT 1984-15-2, Methylenediphosphonic acid 7414-83-7,
Etidronate disodium 7722-88-5 14000-31-8, Diphosphate 112319-85-4,
Imidodiphosphate
RL: BAC (Biological activity or effector, except adverse); THU
(**Therapeutic use**); BIOL (Biological study); USES (Uses)
(inorg. pyrophosphates in treatment of diseases related to inappropriate or inadequate ABC protein activity)

IT 56-65-5, Adenosine triphosphate, biological studies 16887-00-6,
Chloride, biological studies 53696-59-6, 8-Azidoadenosine triphosphate
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(inorg. pyrophosphates in treatment of diseases related to inappropriate or inadequate ABC protein activity)

IT 1984-15-2, Methylenediphosphonic acid
RL: BAC (Biological activity or effector, except adverse); THU
(**Therapeutic use**); BIOL (Biological study); USES (Uses)
(inorg. pyrophosphates in treatment of diseases related to inappropriate or inadequate ABC protein activity)

RN 1984-15-2 HCAPLUS

CN Phosphonic acid, methylenebis- (9CI) (CA INDEX NAME)

H₂O₃P-CH₂-PO₃H₂

L137 ANSWER 15 OF 35 HCAPLUS COPYRIGHT 2001 ACS

AN 1997:467046 HCAPLUS

DN 127:130960

TI Etidronate versus fluoride for treatment of osteopenia in **primary biliary cirrhosis**: preliminary results after 2 years

AU Guanabens, Nuria; Pares, Albert; Monegal, Ana; Peris, Pilar; Pons, Francesca; Alvarez, Luisa; De Osaba, M. Jesus Martinez; Roca, Merce; Torra, Merce; Rodes, Joan

CS Metabolic Bone Diseases Unit, Hospital Clinic i Provincial, University of Barcelona, Barcelona, Spain

SO Gastroenterology (1997), 113(1), 219-224
CODEN: GASTAB; ISSN: 0016-5085

PB Saunders

DT Journal

LA English

CC 1-12 (Pharmacology)

AB Because osteopenia increases morbidity of **primary biliary cirrhosis** (PBC), the effects of cyclical etidronate vs. sodium fluoride on bone mass were compared in patients with PBC. Thirty-two women with PBC were randomly assigned to receive etidronate (400 mg/day during 14 days every 3 mo) or fluoride (50 mg/day, enteric-coated tablets). Bone mineral d. of the lumbar spine and proximal femur were measured initially and every 6 mo. Bone fractures were also evaluated. Sixteen patients were allocated into each group, which were comparable with respect to the severity of PBC and osteopenia. Thirteen patients with etidronate and 10 patients with fluoride completed 2 yr in the study. In the etidronate group, bone mineral d. increased in the lumbar spine (P = 0.02) and did not change in the proximal femur. In the fluoride group, lumbar bone mineral d. did not change but femoral bone mass decreased, particularly in the Ward's triangle. Two patients in the fluoride and none in the etidronate group developed new vertebral fractures, and the no. of new nonvertebral fractures was similar in both groups. Neither treatment impaired liver function or cholestasis. Cyclical etidronate is more effective and better tolerated than sodium fluoride in preventing bone loss in PBC.

ST etidronate fluoride osteopenia bone loss cirrhosis

IT **Cirrhosis (liver)**

(**biliary**; etidronate vs. fluoride for treatment of osteopenia in **primary biliary cirrhosis**)

IT Osteopenia

(etidronate vs. fluoride for treatment of osteopenia in **primary biliary cirrhosis**)

IT 2809-21-4 16984-48-8, Fluoride, biological studies

RL: BAC (Biological activity or effector, except adverse); THU

(**Therapeutic use**); BIOL (Biological study); USES (Uses)

(etidronate vs. fluoride for treatment of osteopenia in **primary biliary cirrhosis**)

IT 2809-21-4

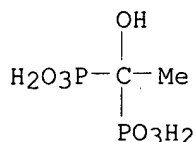
RL: BAC (Biological activity or effector, except adverse); THU

(**Therapeutic use**); BIOL (Biological study); USES (Uses)

(etidronate vs. fluoride for treatment of osteopenia in **primary biliary cirrhosis**)

RN 2809-21-4 HCAPLUS

CN Phosphonic acid, (1-hydroxyethylidene)bis- (9CI) (CA INDEX NAME)



L137 ANSWER 16 OF 35 HCAPLUS COPYRIGHT 2001 ACS

AN 1997:287320 HCAPLUS

DN 126:347199

TI Apoptotic cell death in activated monocytes following incorporation of clodronate-liposomes. Reply to comments

AU Schmidt-Weber, C. B.; Rittig, M.; Hauser, I.; Nurnberg, E.; Emmrich, F.; Palombo-Kinne, E.; Kinne, R. W.

CS Dep. of Pathology, Immunology Research Division, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA

SO J. Leukocyte Biol. (1997), 61(5), 644-645

CODEN: JLBIE7; ISSN: 0741-5400

PB Federation of American Societies for Experimental Biology

DT Journal

LA English

CC 63-5 (Pharmaceuticals)

Section cross-reference(s): 1, 15

AB While the treatment of anatomically confined pathologies such as cancer heavily relies on liposome formulations that evade the mononuclear phagocyte system and thereby increase the availability of drug-laden liposomes to these masses, treatment of systemic inflammatory diseases may instead benefit from the use of liposomes that remain "visible" to the MPS and, in particular, to centrally located macrophage subpopulations with immunoregulatory potential.

ST clodronate liposome monocyte apoptosis **autoimmunity** polemic

IT Antiarthritics

Arthritis

Autoimmune diseases

Liposomes (drug delivery systems)

Macrophage

Monocyte

(apoptotic cell death in activated monocytes following incorporation of clodronate-liposomes)

IT 10596-23-3, Clodronic acid

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)

(apoptotic cell death in activated monocytes following incorporation of clodronate-liposomes)

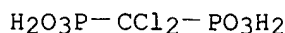
IT 10596-23-3, Clodronic acid

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)

(apoptotic cell death in activated monocytes following incorporation of clodronate-liposomes)

RN 10596-23-3 HCAPLUS

CN Phosphonic acid, (dichloromethylene)bis- (9CI) (CA INDEX NAME)



L137 ANSWER 17 OF 35 HCAPLUS COPYRIGHT 2001 ACS

AN 1997:180436 HCAPLUS

DN 126:220689

TI Cyclical etidronate in the prevention of bone loss in corticosteroid-

treated **primary biliary cirrhosis**: a prospective, controlled pilot study

AU Wolfhagen, Frank H. J.; Van Buuren, Henk R.; Den Ouden, Janny W.; Hop, Wim
 CS C. J.; Van Leeuwen, Johannes P. T. M.; Schalm, Solko W.; Pols, Huib A. P.
 Department of Internal Medicine II (section Hepatology), University
 Hospital Rotterdam, Rotterdam, Neth.
 SO J. Hepatol. (1997), 26(2), 325-330
 CODEN: JOHEEC; ISSN: 0168-8278
 PB Munksgaard
 DT Journal
 LA English
 CC 1-12 (Pharmacology)
 Section cross-reference(s): 2

AB Recently, promising disease modifying effects of low dose corticosteroid treatment in **primary biliary cirrhosis** have been reported. However, steroid-induced bone loss constitutes a potential draw-back of this treatment option. To assess whether etidronate can reduce bone loss during corticosteroid treatment. Twelve **primary biliary cirrhosis** patients (all Child-Pugh Class A), treated with prednisone in the context of a 1-yr placebo-controlled pilot study with prednisone (maintenance dose 10 mg daily), and azathioprine (50 mg daily), were randomized to receive either cyclical etidronate (400 mg daily, during 2 wk) alternated with calcium 500 mg daily during 11 wk or calcium alone. All patients had been receiving ursodeoxycholic acid during at least 1 yr and this treatment was continued. Bone mass was measured in the lumbar spine and the femoral neck by dual energy X-ray absorptiometry before and after 3 and 12 mo of treatment. Markers of bone formation (serum osteocalcin, procollagen-I-propeptide) and bone resorption (urinary deoxypyridinoline and calcium) were also monitored. The mean lumbar bone mineral d. did not significantly change in the patients taking etidronate+calcium, in contrast to patients treated with calcium alone (+0.4 vs. -3.0%; p=0.01). Changes in femoral bone mineral d. and markers of bone turnover did not significantly differ between both groups. No adverse effects of etidronate were noted. Cyclical etidronate appears to prevent bone loss assocd. with prednisone treatment in patients with **primary biliary cirrhosis**. These preliminary results encourage the further evaluation of long term prednisone treatment and concurrent bisphosphonate therapy in **primary biliary cirrhosis**.

ST bone loss corticosteroid biliary cirrhosis etidronate
 IT Bone demineralization
Primary biliary cirrhosis
 (cyclical etidronate in prevention of bone loss in corticosteroid-treated **primary biliary cirrhosis**)

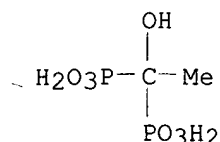
IT Corticosteroids, biological studies
 RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (cyclical etidronate in prevention of bone loss in corticosteroid-treated **primary biliary cirrhosis**)

IT 53-03-2, Prednisone
 RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (cyclical etidronate in prevention of bone loss in corticosteroid-treated **primary biliary cirrhosis**)

IT 128-13-2, Ursodeoxycholic acid 446-86-6, Azathioprine 2809-21-4
 7440-70-2, Calcium, biological studies
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (cyclical etidronate in prevention of bone loss in corticosteroid-treated **primary biliary cirrhosis**)

IT 2809-21-4
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (cyclical etidronate in prevention of bone loss in corticosteroid-treated **primary biliary cirrhosis**)

RN 2809-21-4 HCAPLUS
 CN Phosphonic acid, (1-hydroxyethylidene)bis- (9CI) (CA INDEX NAME)



L137 ANSWER 18 OF 35 HCAPLUS COPYRIGHT 2001 ACS

AN 1997:82270 HCAPLUS

DN 126:181022

TI A double-blind placebo-controlled study to determine the effects of risedronate on bone loss in glucocorticoid-treated rheumatoid arthritis

AU Eastell, R.; Devogelaer, J. P.; Peel, N. F. A.; Gill, C.; Bax, D. E.; Nagant de Deuxchaisnes, C.; Russell, R. G. G.

CS Dep. Human Metabolism Clin. Biochem., Univ. Sheffield, Sheffield, S5 7AU, UK

SO Int. Congr. Ser. (1996), 1118 (Osteoporosis 1996), 391-393

CODEN: EXMDA4; ISSN: 0531-5131

PB Elsevier

DT Journal

LA English

CC 1-7 (Pharmacology)

Section cross-reference(s): 2

AB Glucocorticoid therapy and rheumatoid arthritis are two independent risk factors for osteoporosis resulting together in a 6-fold increase in the risk of vertebral fractures. We performed a double-blinded, placebo-controlled trial of risedronate in 120 postmenopausal women with rheumatoid arthritis on glucocorticoids. Risedronate was given either continuously (2.5 mg/day) or cyclically (15 mg/day for 2 out of 12 wk). At 2 yr there was marked bone loss from the proximal femur in placebo-treated patients. This as well as the bone loss from the spine appeared to be prevented by risedronate treatment.

ST rheumatoid arthritis glucocorticoid bone loss risedronate; osteoporosis rheumatoid arthritis glucocorticoid therapy

IT Antirheumatic drugs

Osteoporosis

Postmenopause

Rheumatoid arthritis

(a double-blind placebo-controlled study to det. the effects of risedronate on bone loss in glucocorticoid-treated rheumatoid arthritis)

IT Glucocorticoids

RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(a double-blind placebo-controlled study to det. the effects of risedronate on bone loss in glucocorticoid-treated rheumatoid arthritis)

IT 105462-24-6

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(a double-blind placebo-controlled study to det. the effects of risedronate on bone loss in glucocorticoid-treated rheumatoid arthritis)

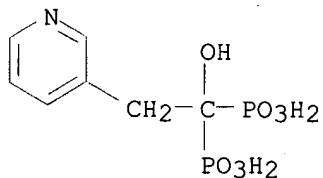
IT 105462-24-6

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

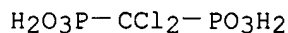
(a double-blind placebo-controlled study to det. the effects of risedronate on bone loss in glucocorticoid-treated rheumatoid arthritis)

RN 105462-24-6 HCAPLUS

CN Phosphonic acid, [1-hydroxy-2-(3-pyridinyl)ethylidene]bis- (9CI) (CA INDEX NAME)



L137 ANSWER 19 OF 35 HCAPLUS COPYRIGHT 2001 ACS
 AN 1996:686835 HCAPLUS
 DN 126:102239
 TI Malignant hematological diseases
 AU Eto, Sumiya
 CS Univ. Occup. Environ. Health, Kitakyushu, 807, Japan
 SO Bone (Osaka) (1996), 10(2), 143-149
 CODEN: BONEFN; ISSN: 0914-7047
 PB Medikaru Rebyusha
 DT Journal; General Review
 LA Japanese
 CC 14-0 (Mammalian Pathological Biochemistry)
 Section cross-reference(s): 1, 3, 15
 AB A review, with 33 refs., on the osteolytic lesions, hypercalcemia and bone-resorbing cytokines in multiple myeloma, adult T-cell leukemia, malignant lymphoma and **pernicious anemia**, and effects of biphosphonates.
 ST review hematol disease cytokine therapy
 IT Adult T-cell leukemia
 Hypercalcemia
 Lymphoma
 Multiple myeloma
 (malignant hematol. diseases and therapies in human)
 IT Interleukin 1
 Interleukin 6
 Tumor necrosis factor .alpha.
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BIOL (Biological study); PROC (Process)
 (malignant hematol. diseases and therapies in human)
 IT **Anemia (disease)**
 (**pernicious anemia**; malignant hematol. diseases and therapies in human)
 IT 7440-70-2, Calcium, biological studies
 RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PROC (Process)
 (malignant hematol. diseases and therapies in human)
 IT 103370-86-1, Humoral hypercalcemic factor
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BIOL (Biological study); PROC (Process)
 (malignant hematol. diseases and therapies in human)
 IT **10596-23-3 40391-99-9**
 RL: BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
 (malignant hematol. diseases and therapies in human)
 IT **10596-23-3**
 RL: BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
 (malignant hematol. diseases and therapies in human)
 RN 10596-23-3 HCAPLUS
 CN Phosphonic acid, (dichloromethylene)bis- (9CI) (CA INDEX NAME)



L137 ANSWER 20 OF 35 HCAPLUS COPYRIGHT 2001 ACS

AN 1996:542252 HCAPLUS

DN 125:230474

TI Apoptotic cell death in activated monocytes following incorporation of clodronate-liposomes

AU Schmidt-Weber, Carsten; Rittig, Michael; Buchner, Eberhard; Hauser, Ingeborg; Schmidt, Irina; Palombo-Kinne, Ernesta; Emmrich, Frank; Kinne, Raimund W.

CS Immunol. Unit, Dep. Medicine III, Univ. Erlangen-Nuremberg, Leipzig, Germany

SO J. Leukocyte Biol. (1996), 60(2), 230-244

CODEN: JLBIE7; ISSN: 0741-5400

DT Journal

LA English

CC 63-5 (Pharmaceuticals)

Section cross-reference(s): 1, 15

AB The present study was performed to elucidate whether sterically stabilized liposomes laden with clodronate, which lead to depletion of macrophages (M.PHI.s) and amelioration of exptl. **autoimmune** arthritis in vivo, selectively affect cells of the m.PHI. lineage in vitro. The rates of incorporation of drug-free, fluorescent liposomes and the rates of cell death following exposure to clodronate-liposomes were assessed in human peripheral blood monocytes, as well as in polymorphonuclear leukocytes (PMNs), T cells, endothelial cells, and fibroblasts, both at rest and following activation. Gel electrophoresis of nuclear exts. and ultrastructural analyses were performed to identify the modality of cell death. Monocytes, particularly upon activation, were ore efficient in incorporating sterically stabilized liposomes than all other cells except PMNs. Twenty percent of resting monocytes and up to 65% of activated monocytes died within 24 h of exposure to clodronate-liposomes, whereas the other cell types, including PMNs, remained unaffected. Activated monocytes exposed to clodronate-liposomes, but not resting or activated monocytes exposed to drug-free liposomes, showed clear signs of apoptotic cell death. In most of the assays, sterically stabilized liposomes were more efficient than conventional phosphatidylcholine-liposomes. Sterically stabilized clodronate-liposomes preferentially affect cells of the m.PHI. lineage, particularly if activated. Selective elimination of activated M.PHI.s by apoptosis may explain both therapeutic efficacy and safety of clodronate-liposomes in exptl. models of **autoimmunity**.

ST clodronate liposome monocyte apoptosis **autoimmunity**

IT Arthritis

Autoimmune disease

Macrophage

Monocyte

(apoptotic cell death in activated monocytes following incorporation of clodronate-liposomes)

IT Inflammation inhibitors

(antiarthritics, apoptotic cell death in activated monocytes following incorporation of clodronate-liposomes)

IT Pharmaceutical dosage forms

(liposomes, apoptotic cell death in activated monocytes following incorporation of clodronate-liposomes)

IT 10596-23-3, Clodronic acid

RL: BAC (Biological activity or effector, except adverse); THU

(**Therapeutic use**); BIOL (Biological study); USES (Uses)

(apoptotic cell death in activated monocytes following incorporation of clodronate-liposomes)

IT 10596-23-3, Clodronic acid

RL: BAC (Biological activity or effector, except adverse); THU

(**Therapeutic use**); BIOL (Biological study); USES (Uses)

(apoptotic cell death in activated monocytes following incorporation of clodronate-liposomes)

RN 10596-23-3 HCAPLUS

CN Phosphonic acid, (dichloromethylene)bis- (9CI) (CA INDEX NAME)

H₂O₃P-CCl₂-PO₃H₂

L137 ANSWER 21 OF 35 HCAPLUS COPYRIGHT 2001 ACS

AN 1996:162133 HCAPLUS

DN 124:250876

TI Effects of HEBP on experimental osteoporosis in ovariectomized rats and streptozotocin-induced diabetic rats

AU Shibata, Hiroyoshi

CS School Dentistry, Aichi-Gakuin University, Japan

SO Aichi Gakuin Daigaku Shigakkaishi (1995), 33(4), 795-811

CODEN: AGDSAB; ISSN: 0044-6912

DT Journal

LA Japanese

CC 1-12 (Pharmacology)

AB Effects of long term administrations of HEBP (1-hydroxyethylidene-1,1-bisphosphonate) at a dose of 0, 2, 4 or 8 mg/kg, every other day on osteoporosis in ovariectomized (OVX) rats, model of high turnover osteoporosis and streptozotocin-induced diabetic (STZD) rats, model of low turnover osteoporosis were examd. OVX rats and STZD rats were administered HEBP for 3 and 2 mo, resp. Tibia, femur and incisor dentin were investigated by chem. analyses and contact microradiog. (CMR). In both OVX and STZD rats, bone loss was obsd. in ash content per unit bone vol. and in CMR of proximal tibia. The bone loss in OVX rats was improved by HEBP at a dose of 2 mg/kg and was partially improved at 4 mg/kg. At a dose of 8 mg/kg, however, HEBP did not improve the bone loss but, rather, potentiated it. In STZD rats, HEBP at a dose of 8 mg/kg increased bone d. At doses of 2 and 4 mg/kg, HEBP had no significant effect on bone loss in STZD rats. These findings indicated that HEBP, well known to inhibit bone resorption as well as mineralization of hard tissues, had a greater effect on bone in OVX rats than STZD rats. Dentin mineralization was not influenced by ovariectomy or streptozotocin treatment. Furthermore, the mineralization in OVX and STZD rats was inhibited dose-dependently to the same degree. Thus, there was no difference in the effect of HEBP on the mineralization in incisor dentin between OVX rats and STZD rats. These results indicated that the effect of HEBP on bone loss was greater in high turnover osteoporosis than in low turnover osteoporosis, and this effect may be based upon the osteoblastic activity in both groups of exptl. animals.

ST osteoporosis hydroxyethylidene bisphosphonate

IT **Diabetes mellitus**

Osteoporosis

(effects of HEBP on exptl. osteoporosis in ovariectomized rats and diabetic rats)

IT 2809-21-4

RL: BAC (Biological activity or effector, except adverse); THU

(**Therapeutic use**); BIOL (Biological study); USES (Uses)

(effects of HEBP on exptl. osteoporosis in ovariectomized rats and diabetic rats)

IT 2809-21-4

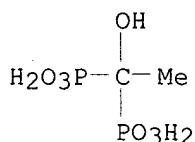
RL: BAC (Biological activity or effector, except adverse); THU

(**Therapeutic use**); BIOL (Biological study); USES (Uses)

(effects of HEBP on exptl. osteoporosis in ovariectomized rats and diabetic rats)

RN 2809-21-4 HCAPLUS

CN Phosphonic acid, (1-hydroxyethylidene)bis- (9CI) (CA INDEX NAME)



L137 ANSWER 22 OF 35 HCAPLUS COPYRIGHT 2001 ACS

AN 1995:926080 HCAPLUS

DN 123:330037

TI Agents for inhibiting DNA biosynthesis with improved membrane-permeating properties

IN Zeppezauer, Michael; Nyman, Per Olaf; Zalud, Petra; Wachs, Wolfgang Oliver

PA Germany

SO Ger. Offen., 20 pp.

CODEN: GWXXBX

DT Patent

LA German

IC ICM C07H019-10

ICS A61K031-70

CC 1-12 (Pharmacology)

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 4341161	A1	19950608	DE 1993-4341161	19931202 <--
	WO 9515332	A1	19950608	WO 1994-EP3969	19941130 <--

W: CA, JP, US

RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRAI DE 1993-4341161 19931202 <--

AB dUTP analogs which interact with dUTPase similarly to dUTP and disrupt DNA biosynthesis are claimed. Preferred are dUTP analogs in which the O between the .alpha.- and .beta.-phosphate group has been replaced by CH2, NH, or S. 2'-Deoxyuridine-5'-.alpha.,.beta.-methylenetriphosphate monobenzyl ester inhibited OH 77 and EG 463 cell growth at 10 .mu.g/mL.

ST deoxyuridine triphosphate analog DNA biosynthesis inhibitor; cytotoxicity deoxyuridine triphosphate analog; cell proliferation inhibitor deoxyuridine triphosphate analog

IT Neoplasm inhibitors

Virucides and Virustats

(deoxyuridine triphosphate analogs as DNA biosynthesis inhibitors)

IT Deoxyribonucleic acids

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(deoxyuridine triphosphate analogs as DNA biosynthesis inhibitors)

IT Autoimmune disease

(inhibitors; deoxyuridine triphosphate analogs as DNA biosynthesis inhibitors)

IT 170428-83-8 170428-84-9 170428-85-0 170428-86-1

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(deoxyuridine triphosphate analogs as DNA biosynthesis inhibitors)

IT 1173-82-6, Deoxyuridine triphosphate

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(deoxyuridine triphosphate analogs as DNA biosynthesis inhibitors)

IT 37289-34-2, Deoxyuridine triphosphatase

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(inhibitors; deoxyuridine triphosphate analogs as DNA biosynthesis inhibitors)

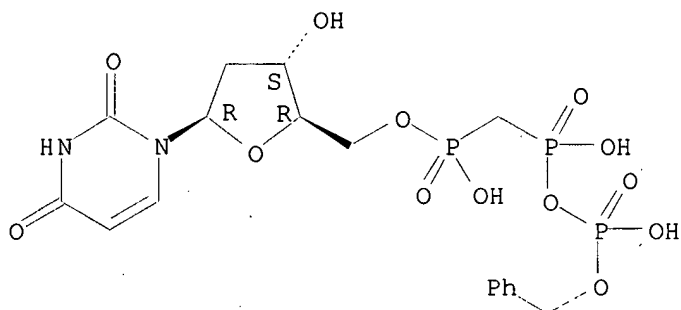
IT 170428-83-8

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(deoxyuridine triphosphate analogs as DNA biosynthesis inhibitors)

RN 170428-83-8 HCAPLUS
 CN Uridine, 2'-deoxy-, 5'-[hydrogen (2,4-dihydroxy-2,4-dioxido-6-phenyl-3,5-dioxa-2,4-diphosphahex-1-yl)phosphonate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L137 ANSWER 23 OF 35 HCAPLUS COPYRIGHT 2001 ACS

AN 1995:781303 HCAPLUS

TI Left ventricular hemodynamic parameters in the course of acute experimental coxsackievirus B 3 **myocarditis**

AU Herzum, Matthias; Weller, Rita; **Jomaa, Hassan**; Wietrzychowski, Frank; Pankuweit, Sabine; Mahr, Peter; Maisch, Bernhard

CS Division of Cardiology, Philipps Univ., Marburg, 35043, Germany

SO J. Mol. Cell. Cardiol. (1995), 27(8), 1573-80

CODEN: JMCDAY; ISSN: 0022-2828

PB Academic

DT Journal

LA English

AB In susceptible DBA/2 mice coxsackievirus B 3-induced **myocarditis** leads to inflammatory and necrotic lesions in the myocardium 7-10 days after virus inoculation. The purpose of this study was to det. whether hemodynamic changes occur in murine coxsackievirus B 3 **myocarditis** and whether they are correlated to histol. cardiac lesions throughout the infection. Left ventricular function was detd. by open chest puncture of the left ventricle in the course of acute coxsackievirus B 3 infection. Histol. cross sections of the heart were stained with hematoxylin/eosin and scored blindly for **myocarditic** lesions. Left ventricular function was preserved until day 7 post-virus inoculation. Left ventricular systolic pressure, +dP/dtmax and -dP/dtmax and heart rate declined significantly from day 7 to day 10. The decrease in these parameters did not correlate with viral concns. in the heart on the day of hemodynamic measurements. The decrease was related to histol. changes on day 10, but not on day 7 of the infection. The data suggest (a) that a cumulative loss of cardiac myofibers, induced either by the virus and/or by immune reactions to the heart, is likely to lead to a late depression of cardiac function, and (b) that there is a weak and only temporary structure-function relationship in the heart in coxsackievirus B 3 **myocarditis**. Therefore, in addn. to an anal. of histol. changes, the measurement of cardiac function appears to be very important in order to completely evaluate the severity of **myocarditis** and the usefulness of any therapy.

L137 ANSWER 24 OF 35 HCAPLUS COPYRIGHT 2001 ACS

AN 1995:206849 HCAPLUS

DN 122:196796

TI Growth inhibition of macrophage-like and other cell types by liposome-encapsulated, calcium-bound, and free bisphosphonates in vitro

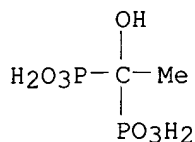
AU Monkkonen, Jukka; Taskinen, Markku; Auriola, Seppo O. K.; Urtti, Arto

CS Dep. Pharmaceutical Technology and A. I. Virtanen Inst., Univ. Kuopio, Kuopio, FIN-70211, Finland

SO J. Drug Targeting (1994), 2(4), 299-308

CODEN: JDTAEH; ISSN: 1061-186X

DT Journal
LA English
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1
AB Bisphosphonates effectively inhibit osteoclastic bone resorption in diseases characterized by excessive bone loss. Liposome-encapsulated clodronate (dichloromethylene bisphosphonate) also is known to inactivate phagocytic cells in vivo, and inhibit the growth of macrophage-like RAW 264 cells in vitro. The macrophage suppressive effect of liposomal clodronate is of interest in **autoimmune** disease, like rheumatoid arthritis, in which phagocytic cells are involved in inflammatory processes. Earlier in vivo studies suggested that liposomal clodronate is a far more potent inactivator of macrophages than liposomal forms of two other bisphosphonate compds., pamidronate (3-amino-1-hydroxypropylidene bisphosphonate), and etidronate (1-hydroxyethylidene-1,1-bisphosphonate). The authors examd. the growth inhibitory properties of these three bisphosphonates encapsulated in liposomes effectively inhibited the growth of RAW 264 and CV1-P cells, while free drugs were 20-1000 times less potent growth inhibitors. Also, high extracellular calcium concns. enhanced the potency of bisphosphonates for RAW 264 cells, indicating that, in addn. to liposomes, the uptake of bisphosphonates by macrophages is mediated also by calcium. In all formulations, pamidronate was the most potent compd. for the cells, with the exception of CV1-P cells, for which liposomal clodronate was the most potent. The effects of liposomal drugs were selective for highly endocytotic cells. The results suggest that liposome-encapsulated bisphosphonates could provide a specific tool to affect the function of macrophages and all three of these bisphosphonates are potentially effective as macrophage suppressors in **autoimmune** diseases.
ST macrophage suppressor liposome encapsulated bisphosphonate calcium
IT **Autoimmune disease**
Liposome
Macrophage
(growth inhibition of macrophage-like and other cell types by liposome-encapsulated, calcium-bound, and free bisphosphonates in vitro)
IT Pharmaceutical dosage forms
(liposomes, growth inhibition of macrophage-like and other cell types by liposome-encapsulated, calcium-bound, and free bisphosphonates in vitro)
IT 2809-21-4 10596-23-3 40391-99-9
RL: BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(growth inhibition of macrophage-like and other cell types by liposome-encapsulated, calcium-bound, and free bisphosphonates in vitro)
IT 7440-70-2, Calcium, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(growth inhibition of macrophage-like and other cell types by liposome-encapsulated, calcium-bound, and free bisphosphonates in vitro)
IT 4537-78-4, Distearoylphosphatidylglycerol
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(growth inhibition of macrophage-like and other cell types by liposome-encapsulated, calcium-bound, and free bisphosphonates in vitro)
IT 2809-21-4
RL: BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(growth inhibition of macrophage-like and other cell types by liposome-encapsulated, calcium-bound, and free bisphosphonates in vitro)
RN 2809-21-4 HCAPLUS
CN Phosphonic acid, (1-hydroxyethylidene)bis- (9CI) (CA INDEX NAME)



L137 ANSWER 25 OF 35 HCAPLUS COPYRIGHT 2001 ACS

AN 1994:208165 HCAPLUS

DN 120:208165

TI Clodronate (dichloromethylene bisphosphonate) inhibits LPS-stimulated IL-6 and TNF production by raw 264 cells

AU Monkkonen, Jukka; Pennanen, Niina; Lapinjoki, Seppo; Urtti, Arto

CS A. I. Virtanen Inst., Univ. Kuopio, Kuopio, FIN-70211, Finland

SO Life Sci. (1994), 54(14), PL229-PL234

CODEN: LIFSAK; ISSN: 0024-3205

DT Journal

LA English

CC 1-7 (Pharmacology)

Section cross-reference(s): 63

AB The effect of liposome-encapsulated and free clodronate on the IL-6 and TNF prodn. by macrophages was studied using RAW 264 cell line as a macrophage model, and disocn.-enhanced lanthanide fluoroimmunoassay (DELFI) for anal. of secreted cytokines. LPS (lipopolysaccharide)-stimulated RAW 264 cells proved to produce notable amts. of these two cytokines, and DELFI was sensitive and reliable method for anal. Liposome-encapsulated clodronate inhibited the prodn. of both cytokines, IL-6 being affected more than TNF, and the effect was mostly due to the drug itself, not to liposomal lipid. More than ten times higher concn. of free clodronate than liposomal clodronate was needed to inhibit cytokine prodn. This is the first report on the cytokine inhibitory property of clodronate, and the results support the idea of the use of liposomal clodronate as a macrophage suppressive agent in **autoimmune** diseases.

ST clodronate interleukin tumor necrosis factor macrophage; interleukin 6 macrophage clodronate

IT Immunosuppressants

(clodronate inhibition of interleukin 6 and tumor necrosis factor in macrophages in relation to)

IT Macrophage

(interleukin 6 and tumor necrosis factor formation stimulation by lipopolysaccharides in, free and liposome-encapsulated clodronate inhibition of)

IT Lipopolysaccharides

RL: BIOL (Biological study)

(interleukin 6 and tumor necrosis factor formation stimulation by, in macrophages, free and liposome-encapsulated clodronate inhibition of)

IT Lymphokines and Cytokines

RL: FORM (Formation, nonpreparative)

(interleukin 6, formation of, by macrophages, free and liposome-encapsulated clodronate inhibition of lipopolysaccharide-stimulated)

IT Pharmaceutical dosage forms

(liposomes, for clodronate, interleukin 6 and tumor necrosis factor stimulated by lipopolysaccharides in macrophages inhibition by)

IT Lymphokines and Cytokines

RL: FORM (Formation, nonpreparative)

(tumor necrosis factor, formation of, by macrophages, free and liposome-encapsulated clodronate inhibition of lipopolysaccharide-stimulated)

IT 10596-23-3, Clodronate

RL: BIOL (Biological study)

(interleukin 6 and tumor necrosis factor stimulated by lipopolysaccharides in macrophages inhibition by free and

liposome-encapsulated)
 IT 10596-23-3, Clodronate
 RL: BIOL (Biological study)
 (interleukin 6 and tumor necrosis factor stimulated by
 lipopolysaccharides in macrophages inhibition by free and
 liposome-encapsulated)
 RN 10596-23-3 HCAPLUS
 CN Phosphonic acid, (dichloromethylene)bis- (9CI) (CA INDEX NAME)

H₂O₃P-CCl₂-PO₃H₂

L137 ANSWER 26 OF 35 HCAPLUS COPYRIGHT 2001 ACS
 AN 1994:153244 HCAPLUS
 DN 120:153244
 TI Selective elimination of macrophages by dichlormethylene
 diphosphonate-containing liposomes suppresses experimental
autoimmune neuritis
 AU Jung, Stefan; Huitinga, Ingeborg; Schmidt, Beate; Zielasek, Juergen;
 Dijkstra, Christine D.; Toyka, Klaus V.; Hartung, Hans Peter
 CS Dep. Neurol., Julius-Maximilians-Univ., Wurzburg, Germany
 SO J. Neurol. Sci. (1993), 119(2), 195-202
 CODEN: JNSCAG; ISSN: 0022-510X
 DT Journal
 LA English
 CC 1-7 (Pharmacology)
 AB The injection of liposome-encapsulated dichlormethylene diphosphonate
 (Cl2MDP) constitutes an effective method to selectively eliminate
 phagocytic cells from spleen, liver and the circulation. The authors
 evaluated the effect of Cl2MDP-liposomes on the course of actively induced
 and adoptively transferred exptl. **autoimmune** neuritis (EAN),
 both animal models of the human Guillain-Barre syndrome. Injection of
 Cl2MDP-liposomes 11 and 13 days post-immunization (p.i.) of Lewis rats
 with bovine peripheral nerve myelin efficiently prevented clin. signs of
 EAN up to day 15 p.i., when all control animals were affected.
 Thereafter, EAN gradually also developed in Cl2MDP-liposome-treated rats,
 but until day 19, disease was significantly milder than in control rats
 injected with buffer-filled liposomes. Adoptive transfer EAN (AT-EAN)
 induced by injection of activated P2-specific T cells could be suppressed
 even more markedly by application of Cl2MDP-liposomes 1, 3, and 6 days
 after cell transfer. Efficient suppression of AT-EAN by Cl2MDP-liposomes
 rules out the possibility that EAN is prevented due to interference with
 the induction phase of this exptl. disease and confirms that macrophages
 are important effector cells during EAN. Selective suppression of
 phagocytic cell function by drug-contg. liposomes may hold promise as a
 novel treatment of demyelinating **autoimmune** diseases of the
 nervous system.
 ST dichlormethylene diphosphonate liposome **autoimmune** neuritis
 macrophage
 IT Macrophage
 (autoimmune neuritis treatment with dichlormethylene
 diphosphonate-contg. liposomes in relation to inhibition of)
 IT Nervous system
 (disease, Guillain-Barre syndrome, dichlormethylene
 diphosphonate-contg. liposomes for treatment of, macrophages inhibition
 in relation to)
 IT Pharmaceutical dosage forms
 (liposomes, dichlormethylene diphosphonate-contg., **autoimmune**
 neuritis treatment with, macrophages inhibition in)
 IT Nerve, disease
 (neuritis, **autoimmune**, dichlormethylene diphosphonate-contg.
 liposomes treatment of, macrophages inhibition in relation to)
 IT 10596-23-3
 RL: BIOL (Biological study)

(liposomes contg., **autoimmune** neuritis treatment with,
macrophages inhibition in)
IT 10596-23-3
RL: BIOL (Biological study)
(liposomes contg., **autoimmune** neuritis treatment with,
macrophages inhibition in)
RN 10596-23-3 HCAPLUS
CN Phosphonic acid, (dichloromethylene)bis- (9CI) (CA INDEX NAME)

H₂O₃P-CCl₂-PO₃H₂

L137 ANSWER 27 OF 35 HCAPLUS COPYRIGHT 2001 ACS

AN 1994:124843 HCAPLUS

DN 120:124843

TI The effects of liposome-encapsulated and free clodronate on the growth of
macrophage-like cells in vitro: the role of calcium and iron

AU Monkkonen, Jukka; Heath, Timothy D.

CS Sch. Pharm., Univ. Wisconsin, Madison, WI, 53706, USA

SO Calcif. Tissue Int. (1993), 53(2), 139-46

CODEN: CTINDZ; ISSN: 0171-967X

DT Journal

LA English

CC 1-12 (Pharmacology)

Section cross-reference(s): 63

AB Clodronate (dichloromethylene bisphosphonate) inhibits the activity of
osteoclasts, thereby preventing bone resorption in disorders characterized
by excessive bone loss. I.v. injected clodronate encapsulated in
liposomes is also known to inactivate phagocytic cells in spleen and liver
in vivo. The macrophage suppressive effect of clodronate is of interest
in **autoimmune** diseases, like rheumatoid arthritis, in which
phagocytic cells are involved in inflammatory processes, but knowledge of
the interaction of clodronate with phagocytic cells is scarce. The
authors have studied the uptake of clodronate, both free and encapsulated
in neg. charged liposomes, by the macrophage-like cell line RAW 264 and by
other types of cell lines. The uptake was assessed by a growth inhibition
assay. The liposome-encapsulated clodronate was 50 and 350 times more
potent than free drug for RAW 264 and CV1-P, resp. Cell lines with a
lower endocytic capacity were insensitive to liposome-mediated delivery of
the drug. The action of free clodronate seemed to be extracellular in all
cell lines studied. Calcium and/or iron have been suggested to be
involved in the intracellular uptake and action of clodronate in
phagocytic cells. The authors found that the uptake of free clodronate by
RAW 264 cells was indeed mediated by calcium and iron, while the uptake of
liposomal drugs was only slightly affected by calcium. The increased
intracellular calcium concn. in macrophages did not significantly affect
the growth-inhibitory properties of clodronate, whereas iron loading of
the cells partially restored the cell growth. The data do not support the
role of calcium chelation as a mechanism of action of clodronate, but
suggest that intracellular iron is, at least partially involved.

ST liposome encapsulated clodronate macrophage calcium iron

IT Macrophage

(growth of, liposome-encapsulated clodronate inhibition of, uptake in,
calcium and iron in)

IT Cell proliferation

(of macrophage, liposome-encapsulated clodronate inhibition of, uptake
in, calcium and iron in)

IT Biological transport

(absorption, of liposome-encapsulated clodronate, by macrophage,
calcium and iron in)

IT Pharmaceutical dosage forms

(liposomes, for clodronate, macrophage growth inhibition by and uptake
of, calcium and iron in)

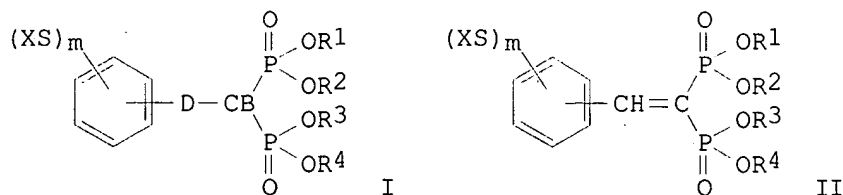
IT 7439-89-6, Iron, biological studies 7440-70-2, Calcium, biological

studies
 RL: BIOL (Biological study)
 (in macrophage growth inhibition and uptake of liposome-encapsulated
 clodronate)
 IT 10596-23-3, Clodronate
 RL: BIOL (Biological study)
 (macrophage growth inhibition by and uptake of, liposome encapsulation
 effect on, calcium and iron in)
 IT 10596-23-3, Clodronate
 RL: BIOL (Biological study)
 (macrophage growth inhibition by and uptake of, liposome encapsulation
 effect on, calcium and iron in)
 RN 10596-23-3 HCAPLUS
 CN Phosphonic acid, (dichloromethylene)bis- (9CI) (CA INDEX NAME)

H₂O₃P-CCl₂-PO₃H₂

L137 ANSWER 28 OF 35 HCAPLUS COPYRIGHT 2001 ACS
 AN 1994:8745 HCAPLUS
 DN 120:8745
 TI Preparation of methanediphosphonic acid derivatives as drugs
 IN Kawabe, Norio; Uchiro, Hiromi; Nakadate, Teruo; Tanahashi, Masahiko; Ito,
 Masatoshi
 PA Toray Industries, Inc., Japan
 SO PCT Int. Appl., 67 pp.
 CODEN: PIXXD2
 DT Patent
 LA Japanese
 IC ICM C07F009-38
 ICS C07F009-40; A61K031-66
 CC 29-7 (Organometallic and Organometalloidal Compounds)
 Section cross-reference(s): 1
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9305052	A1	19930318	WO 1992-JP1140	19920907 <--
W: CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE				
EP 594857	A1	19940504	EP 1992-918702	19920907 <--
EP 594857	B1	19980429		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, SE				
JP 08026048	B4	19960313	JP 1992-504234	19920907 <--
CA 2095128	C	19980106	CA 1992-2095128	19920907 <--
AT 165603	E	19980515	AT 1992-918702	19920907 <--
ES 2114946	T3	19980616	ES 1992-918702	19920907 <--
US 5527940	A	19960618	US 1994-340819	19941117 <--
US 5683992	A	19971104	US 1996-617937	19960315 <--
PRAI JP 1991-226175		19910905 <--		
JP 1992-179802		19920707 <--		
WO 1992-JP1140		19920907 <--		
US 1993-50084		19930428 <--		
US 1994-340819		19941117 <--		
OS MARPAT 120:8745				
GI				



AB The title compds. [I and II; B = H, alkyl, OH, alkoxy, NH₂; D = O, S, (alkyl)imino, OH₂, SCH₂; x = (hetero-substituted) alkyl, aryl, acyl; R₁-R₄ = H, C₁-7 alkyl; m = 1-5], effective in treating inflammation, rheumatism, bone metab. disorders, osteoporosis, **autoimmune** disease, and useful as interleukin-1 inhibitors and antioxidants, are prepd. Grignard reaction of 4-BrC₆H₄SM_e with Mg in THF and subsequent refluxing with cryst. S gave 72% (4-MeSC₆H₄)₂S₂, which was treated with a reaction mixt. of CH₂[P(O)(OEt)₂]₂ and BuLi in THF-hexane to give 41% p-I (R₁-R₄ = Et, B = H, D = S, X = Me, m = 1) (III). Treating III with BrSiMe₃ in CH₂Cl₂ under Ar gave 69% p-I (R₁-R₄ = H, others remain unchanged as in III), which showed antiinflammatory activity at 20 mg/kg in rats, 62.3% inhibition of bone destruction, 51.1% inhibition of interleukin-1 formation, 46.3 .+- . 0.81% inhibition of active O formation, and 79.9 .+- . 3.12% inhibition of bone resorption.

ST methanediphosphonate prepn drug; interleukin 1 inhibitor
methanediphosphonate prepn; antioxidant methanediphosphonate prepn; bone resorption inhibitor methanediphosphonate prepn; antiinflammatory methanediphosphonate prepn; antirheumatic methanediphosphonate prepn; **autoimmune** disease methanediphosphonate prepn

IT Antioxidants

Inflammation inhibitors

(methanediphosphonic acid derivs.)

IT **Autoimmune disease**

Osteoporosis

(treatment of, methanediphosphonic acid derivs. for)

IT Lymphokines and Cytokines

RL: USES (Uses)

(interleukin 1, inhibitors, metanediphosphonic acid derivs.)

IT Bone, disease

(metabolic, treatment of, methanediphosphonic acid derivs. for)

IT 7704-34-9, Sulfur, reactions

RL: RCT (Reactant)

(Grignard reaction of, in prepn. of drugs)

IT 104-95-0, 4-Bromothioanisole

RL: RCT (Reactant)

(Grignard reaction of, with sulfur, in prepn. of drugs)

IT **151425-90-0P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)

(prepn. and hydrolysis of, in prepn. of drugs)

IT 59014-88-9P 84910-80-5P 93972-94-2P 151426-21-0P 151426-22-1P

151426-23-2P 151426-24-3P 151426-25-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)

(prepn. and reaction of, in prepn. of drug)

IT 20057-77-6P, Bis[4-(methylthio)phenyl] disulfide

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)

(prepn. and reaction of, in prepn. of drugs)

IT 151425-91-1P 151425-92-2P 151425-93-3P

151425-94-4P 151425-95-5P 151425-96-6P

151425-97-7P 151425-98-8P 151425-99-9P

151426-00-5P 151426-01-6P 151426-02-7P

151426-03-8P 151426-04-9P 151426-05-0P

151426-06-1P 151426-07-2P 151426-08-3P

151426-09-4P 151426-10-7P 151426-11-8P

151426-12-9P 151426-13-0P 151426-14-1P

151426-15-2P 151426-16-3P 151426-17-4P

151426-18-5P 151426-19-6P 151426-20-9P

151456-40-5P 151456-41-6P

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study);

PREP (Preparation); USES (Uses)

(prepn. of, as drug)

IT 1660-94-2, Tetraethyl methylenediphosphonate

RL: RCT (Reactant)

(reaction of, with bis(methylthiophenyl) disulfide in prepn. of drugs)

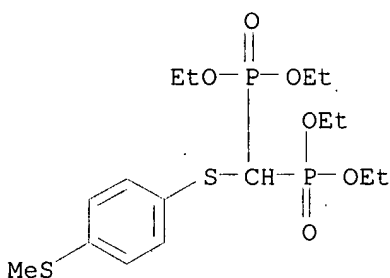
IT 151425-90-0P

RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use)

(prepn. and hydrolysis of, in prepn. of drugs)

RN 151425-90-0 HCAPLUS

CN Phosphonic acid, [[[4-(methylthio)phenyl]thio]methylene]bis-, tetraethyl ester (9CI) (CA INDEX NAME)



L137 ANSWER 29 OF 35 HCAPLUS COPYRIGHT 2001 ACS

AN 1990:491460 HCAPLUS

DN 113:91460

TI Substituted adenine derivatives useful as therapeutic agents

IN Carson, Dennis A.; Carrera, Carlos J.

PA Scripps Clinic and Research Foundation, USA

SO PCT Int. Appl., 70 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM C07H019-19

ICS A61K031-70

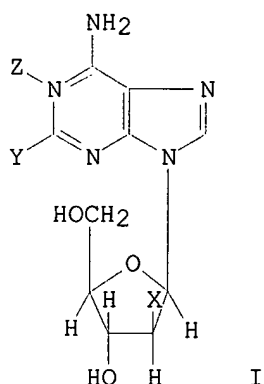
CC 1-7 (Pharmacology)

Section cross-reference(s): 33, 63

FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 8908658	A1	19890921	WO 1989-US1088	19890316 <--
	W: AU, DK, FI, JP, KR, NO				
	RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
	AU 8934105	A1	19891005	AU 1989-34105	19890316 <--
	AU 626296	B2	19920730		
	EP 364559	A1	19900425	EP 1989-904431	19890316 <--
	EP 364559	B1	19950920		
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	JP 03501258	T2	19910322	JP 1989-504299	19890316 <--
	JP 3090456	B2	20000918		
	AT 128141	E	19951015	AT 1989-904431	19890316 <--
	CA 1339964	A1	19980721	CA 1989-593979	19890316 <--
	DK 8905721	A	19891115	DK 1989-5721	19891115 <--
	DK 170629	B1	19951120		
	NO 8904558	A	19891115	NO 1989-4558	19891115 <--
	CA 2191230	AA	19951207	CA 1994-2191230	19940526 <--
	AU 9474707	A1	19951221	AU 1994-74707	19940526 <--
	JP 10505323	T2	19980526	JP 1994-500782	19940526 <--

AU 9918593 A1 19990506 AU 1999-18593 19990304 <--
 PRAI US 1988-169618 19880316 <--
 US 1989-323350 19890314 <--
 WO 1989-US1088 19890316 <--
 AU 1994-74707 19940526 <--
 WO 1994-US5971 19940526 <--
 OS MARPAT 113:91460
 GI



AB Substituted adenine derivs. I (e.g. Z = O or absent; Y = H or a substituent contg. 1-20 atoms that is free from net ionic charge at physiol. pH values; X = H or F; when Z is absent, X = F; Y is H only when Z is present and X = F) are effective in treating **autoimmune** diseases and monocyte-mediated disorders. For treating monocyte-mediated diseases, an antimicrobial agent in addn. to I may be administered. EDs of I for treating monocyte-mediated disease, **autoimmune** disease (i.e. rheumatoid arthritis), and AIDS are claimed. No therapeutic tests are given. In vitro as well as in vivo cytotoxicity of 2-chlorodeoxyadenosine is described. Thus, 2-chloro-9,1'-beta.-2'-deoxy-2'-fluoro-D-arabinofuranosyl adenine (II) was prepd. starting from 1,3'-di-O-acetyl-5'-O-benzoyl-2'-deoxy-2'-fluoro-beta.-D-arabinose via 3'-O-acetyl-5'-O-benzoyl-2'-deoxy-2'-fluoro-D-arabinofuranosyl bromide and 2,6'-dichloro-9,1'-(3'-O-acetyl-5'-O-benzoyl-2'-deoxy-2'-fluoro-beta.-D-arabinofuranosyl)-9-purine. Tablets were prepd. contg. II 1, starch 40, modified starch 10, Mg stearate 1-5 mg and CaHPO4 q.s.

ST adenine deriv pharmaceutical **autoimmune** disease; monocyte mediated disease adenine deriv; AIDS pharmaceutical adenine deriv

IT Interferons
 RL: BIOL (Biological study)
 (AIDS treatment with 2-chloro-2'-deoxyadenosine and)

IT Phagocytosis
 Ribonucleic acid formation
 (by monocyte after exposure to chlorodeoxyadenosine)

IT Immunosuppression
 (by substituted adenine derivs.)

IT Fibroblast
 Lymphocyte
 Monocyte
 Neutrophil
 (chlorodeoxyadenosine cytotoxicity to)

IT Deoxyribonucleic acids
 RL: BIOL (Biological study)
 (damage to, in monocytes after exposure to chlorodeoxyadenosine)

IT Disease
 (monocyte-mediated, treatment of, substituted adenine derivs. for)

IT Pharmaceutical dosage forms

(substituted adenine deriv.-contg., for treating **autoimmune** diseases and monocyte-mediated diseases)

IT Immunodeficiency
(acquired immune deficiency syndrome, treatment of, substituted adenine derivs. for)

IT Inflammation inhibitors
(antiarthritics, substituted adenine derivs. as)

IT Disease
(**autoimmune**, treatment of, substituted adenine derivs. for)

IT Bactericides, Disinfectants, and Antiseptics
Virucides and Virustats
(medical, monocyte-mediated disease treatment with substituted adenine derivs. and)

IT Interferons
RL: PROC (Process)
(.beta.2, release of, by monocyte after exposure to chlorodeoxyadenosine)

IT 7481-89-2, 2',3'-Dideoxycytidine 30516-87-1 59277-89-3, Acyclovir
RL: BIOL (Biological study)
(AIDS treatment with 2-chloro-2'-deoxyadenosine and)

IT 4291-63-8, 2-Chloro-2'-deoxyadenosine
RL: BIOL (Biological study)
(AIDS treatment with azidothymidine and)

IT 53-03-2, Prednisone 54-05-7, Chloroquine 58-14-0, Pyrimethamine 63-74-1 90-34-6, Primaquine 100-33-4 107-36-8 599-79-1, Sulfasalazine 1397-89-3, Amphotericin B **7414-83-7** 8064-90-2 16037-91-5 23256-30-6, Nifurtimox 53230-10-7, Mefloquine 128994-33-2
RL: BIOL (Biological study)
(monocyte-mediated disease treatment with substituted adenine derivs. and)

IT 53-84-9, NAD 56-65-5, ATP, biological studies
RL: BIOL (Biological study)
(of monocytes after exposure to chlorodeoxyadenosine)

IT 4291-63-8 123318-82-1 128994-34-3
RL: BIOL (Biological study)
(pharmaceuticals contg., for treating **autoimmune** and monocyte-mediated diseases)

IT 56632-81-6P 103884-99-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, for therapeutic adenine deriv. prepn.)

IT 3506-01-2P 123318-82-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, for treating **autoimmune** or monocyte-mediated diseasesmonocyte-mediated disease)

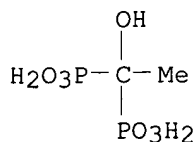
IT 56632-80-5
RL: RCT (Reactant)
(reaction of, for therapeutic adenine deriv. prepn.)

IT 958-09-8, 2'-Deoxyadenosine
RL: RCT (Reactant)
(reaction of, for therapeutic deoxyadenosine oxide prepn.)

IT 5451-40-1, 2,6-Dichloropurine
RL: RCT (Reactant)
(reaction of, with acetylbenzoyldeoxyfluoroarabinofurosyl bromide)

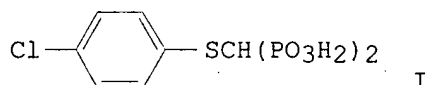
IT **7414-83-7**
RL: BIOL (Biological study)
(monocyte-mediated disease treatment with substituted adenine derivs. and)

RN 7414-83-7 HCAPLUS
CN Phosphonic acid, (1-hydroxyethylidene)bis-, disodium salt (9CI) (CA INDEX NAME)



● 2 Na

L137 ANSWER 30 OF 35 HCAPLUS COPYRIGHT 2001 ACS
 AN 1987:60920 HCAPLUS
 DN 106:60920
 TI Effect of (4-chlorophenyl)thiomethylenebisphosphonic acid (SR 41319) on the **autoimmune** disease activity in MRL/l mice
 AU Barbier, A.; Planchenault, C.; Breliere, J. C.
 CS Clin-Midy Res. Cent., Sanofi Res., Montpellier, 34082, Fr.
 SO Agents Actions (1986), 19(5-6), 311-12
 CODEN: AGACBH; ISSN: 0065-4299
 DT Journal
 LA English
 CC 1-7 (Pharmacology)
 GI



AB MRL-lpr/lpr (MRL/1) mice spontaneously develop an **autoimmune** pathol. including arthritic lesions. SR 41319 (I) [96538-83-9], a bisphosphonate, having previously shown to be active in in vitro and in vivo models of arthritis, was studied for its possible effect on the pathol. of the disease in MRL/1 mice. Results showed that SR 41319 reduced the severity of the disease in its early stages and increased mean life span.
 ST **autoimmune** disease chlorophenylthiomethylenebisphosphonate; SR 41319 **autoimmune** disease
 IT Disease
 (autoimmune, inhibition of, by (chlorophenyl)thiomethylenebisphosphonic acid)
 IT 96538-83-9, SR 41319
 RL: BIOL (Biological study)
 (autoimmune disease inhibition by)
 IT 96538-83-9, SR 41319
 RL: BIOL (Biological study)
 (autoimmune disease inhibition by)
 RN 96538-83-9 HCAPLUS

L137 ANSWER 31 OF 35 HCAPLUS COPYRIGHT 2001 ACS
 AN 1985:404838 HCAPLUS
 DN 103:4838
 TI Comparative study of etidronate and SR 41319, a new diphosphonate, on passive cutaneous anaphylaxis and phospholipase A2 activity
 AU Barbier, A.; Breliere, J. C.; Paul, R.; Roncucci, R.
 CS Cent. Rech. CLIN-MIDY, SANOFI, Montpellier, 34082, Fr.
 SO Agents Actions (1985), 16(1-2), 41-2
 CODEN: AGACBH; ISSN: 0065-4299
 DT Journal
 LA English
 CC 15-9 (Immunochemistry)

Section cross-reference(s): 1

- AB Diphosphonates are known to affect Ca metab. It was therefore of interest to investigate the effects of SR 41319, a new diphosphonate, in comparison with etidronate disodium (EHDP) on passive cutaneous anaphylaxis (PCA) and on phospholipase A2 (PLA2) activity which are both mediated by Ca-dependent mechanisms. Results showed that: (1) i.v., SR 41319 induced a dose-dependent inhibition of PCA more pronounced than that of EHDP; (2) in PLA2 assay, marked inhibition was obtained with SR 41319, whereas EHDP was slightly active. Decrease in Ca entry into mast cells and anti-PLA2 activity of SR 41319 might partly explain the SR 41319 inhibition of PCA.
- ST anaphylaxis phospholipase SR41319 diphosphonate; hypersensitivity treatment SR41319 diphosphonate
- IT Mast cell
(passive cutaneous anaphylaxis and phospholipase A2 of, SR 41319 / diphosphonate effect on)
- IT **Allergy**
(hypersensitivity, treatment of, SR 41319 diphosphonate effects on passive cutaneous anaphylaxis and phospholipase A2 of mast cell in relation to)
- IT Anaphylaxis
(passive cutaneous, SR 41319 diphosphonate effect on, of mast cell)
- IT 7440-70-2, biological studies
RL: BIOL (Biological study)
(SR 41319 diphosphonate effects on passive cutaneous anaphylaxis and phospholipase A2 of mast cell in relation to)
- IT 9001-84-7
RL: BIOL (Biological study)
(of mast cell, SR 41319 effect on)
- IT **96538-83-9**
RL: BIOL (Biological study)
(passive cutaneous anaphylaxis and phospholipase A2 of mast cell response to)
- IT **96538-83-9**
RL: BIOL (Biological study)
(passive cutaneous anaphylaxis and phospholipase A2 of mast cell response to)
- RN 96538-83-9 HCAPLUS

L137 ANSWER 32 OF 35 HCAPLUS COPYRIGHT 2001 ACS

AN 1979:413944 HCAPLUS

DN 91:13944

TI Effect of the diphosphonate EHDP on plasma inorganic phosphate and hemoglobin oxygen affinity of diabetic and healthy subjects

AU Ditzel, Joern; Hau, C.; Daugaard, Niels

CS Dep. Med., Aalborg Reg. Hosp., Aalborg, Den.

SO Adv. Exp. Med. Biol. (1977), 81(Phosphate Metab.), 423-30

CODEN: AEMBAP; ISSN: 0065-2598

DT Journal

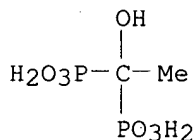
LA English

CC 1-6 (Pharmacodynamics)

Section cross-reference(s): 14

- AB The effect of oral 2Na ethane-1-hydroxy-1,1-diphosphonate (EHDP) [7414-83-7] (20 mg/kg daily) and placebo given for 28 days on plasma inorg. phosphate (Pi), red cell 2,3-diphosphoglycerate [7782-44-7], and O affinity of Hb was evaluated in insulin-treated diabetics and healthy volunteers. EHDP significantly increased mean Pi (diabetics: 1.18-1.67 mmol/L, controls: 1.03-1.71 mmol/L, and the O affinity P50 (pO50 at 50% O satn.) at in vivo pH of the oxyHb disocn. curve (diabetics: 25.4-26.6 mmHg, controls: 26.3-28.9 mmHg). Pi and P50 were correlated in both diabetics and in controls. 2,3-Diphosphoglycerate increased when the diabetics were on EHDP. The study emphasizes the importance of Pi on red cell function and indicates that an elevation of Pi tends to counteract the defect in O release capacity of the red cells in diabetic subjects.
- ST diabetes erythrocyte oxygen phosphate; diphosphonate Hb oxygen diabetes
- IT Blood plasma

- (inorg. phosphate of, in diabetes, diphosphonate effect on, Hb and O affinity in relation to)
- IT Erythrocyte
(inorg. phosphate of, in diabetes, oxygen affinity of Hbs in relation to)
- IT Diabetes mellitus
(oxygen affinity of Hbs in, inorg. phosphate of erythrocyte in relation to)
- IT Hemoglobins
RL: PRP (Properties)
(oxygen affinity of, in diabetes, inorg. phosphate of erythrocytes in relation to)
- IT 7782-44-7, biological studies
RL: PRP (Properties)
(affinity of, in Hbs in diabetes, inorg. phosphate of erythrocytes in relation to)
- IT 7414-83-7
RL: BIOL (Biological study)
(inorg. phosphate of blood plasma and oxygen affinity of Hbs response to, in diabetes)
- IT 7414-83-7
RL: BIOL (Biological study)
(inorg. phosphate of blood plasma and oxygen affinity of Hbs response to, in diabetes)
- RN 7414-83-7 HCAPLUS
- CN Phosphonic acid, (1-hydroxyethylidene)bis-, disodium salt (9CI) (CA INDEX NAME)



● 2 Na

- L137 ANSWER 33 OF 35 HCAPLUS COPYRIGHT 2001 ACS
- AN 1977:594043 HCAPLUS
- DN 87:194043
- TI Methylene diphosphonic acid inhibition of the delayed and immediate types of hypersensitivity in guinea pigs
- AU Komissarenko, S. V.; Zhuravskii, N. I.; Karlova, N. P.; Gulyi, M. F.
- CS A. V. Palladin Inst. Biochem., Kiev, USSR
- SO Byull. Eksp. Biol. Med. (1977), 84(9), 339-41
CODEN: BEBMAE
- DT Journal
- LA Russian
- CC 1-5 (Pharmacodynamics)
- AB Methylene diphosphonic acid [1984-15-2] (30 .mu.g/g) injected s.c. into guinea pigs inhibited both immediate and delayed hypersensitivity to sheep red blood cells.
- ST methylene diphosphonate hypersensitivity; allergy methylene diphosphonate
- IT Allergy
(delayed hypersensitivity, methylene diphosphonate inhibition of)
- IT Allergy
(hypersensitivity, methylene diphosphonate inhibition of)
- IT 1984-15-2
RL: BIOL (Biological study)
(allergy response to)
- IT 1984-15-2

RL: BIOL (Biological study)

(allergy response to)

RN 1984-15-2 HCAPLUS

CN Phosphonic acid, methylenebis- (9CI) (CA INDEX NAME)

H₂O₃P-CH₂-PO₃H₂

L137 ANSWER 34 OF 35 HCAPLUS COPYRIGHT 2001 ACS

AN 1977:527290 HCAPLUS

DN 87:127290

TI The effects of various diphosphonates on a rat model of cardiac calciphylaxis

AU Rosenblum, I. Y.; Black, H. E.; Ferrell, J. F.

CS Miami Val. Lab., Procter and Gamble Co., Cincinnati, Ohio, USA

SO Calcif. Tissue Res. (1977), 23(2), 151-9

CODEN: CATRBZ

DT Journal

LA English

CC 1-5 (Pharmacodynamics)

Section cross-reference(s): 14

AB Seven diphosphonate analogs were tested for their effects on myocardial and cardiovascular degeneration and calcification in an exptl. model of cardiac calciphylaxis. A single oral dose of dihydrotachysterol (DHT) [67-96-9] administered to rats induced myocardial and vascular degeneration, focal **myocarditis** and vasculitis, and myocardial and vascular mineralization. The results demonstrated a considerable variation among the various diphosphonates in their ability to block the pathol. changes obsd. in this model. Ethane-1-hydroxy-1,1-diphosphonic acid (EHDP) [2809-21-4] was the most effective diphosphonate in reducing myocardial and vascular degeneration and calcification, whereas diphosphonates such as ethane-1-amino-1,1-diphosphonic acid (EADP) [15049-85-1] and hydroxymethylene diphosphonic acid (HMDP) [15468-10-7] had little or no effect compared to saline controls. For those diphosphonates which were effective, e.g., EHDP, the tissue-protective effects were obsd. whether the rats were treated with drug prior to the administration of DHT, or whether drug treatment commenced after DHT administration. The results are discussed in terms of the known biol. properties of the diphosphonate drugs.

ST diphosphonate heart calciphylaxis

IT Calciphylaxis

(of heart, diphosphonates effect on)

IT Heart, disease or disorder

(calciphylaxis, diphosphonate effect on)

IT 67-96-9

RL: BIOL (Biological study)

(heart calciphylaxis from, diphosphonates effect on)

IT 1984-15-2 2809-21-4 10596-23-3

15049-85-1 15468-10-7 29712-28-5

34393-98-1 36465-90-4D, analogs

RL: BIOL (Biological study)

(heart calciphylaxis response to)

IT 1984-15-2

RL: BIOL (Biological study)

(heart calciphylaxis response to)

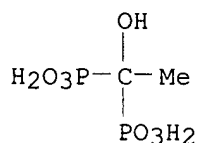
RN 1984-15-2 HCAPLUS

CN Phosphonic acid, methylenebis- (9CI) (CA INDEX NAME)

H₂O₃P-CH₂-PO₃H₂

L137 ANSWER 35 OF 35 HCAPLUS COPYRIGHT 2001 ACS

AN 1977:515854 HCAPLUS
 DN 87:115854
 TI Effect of the diphosphonate ethane-1-hydroxy-1, 1-diphosphonate (EHDP) on hemoglobin oxygen affinity of diabetic and healthy subjects
 AU Ditzel, Joern; Hau, Christian; Daugaard, Niels
 CS Dep. Med., Aalborg Reg. Hosp., Aalborg, Den.
 SO Microvasc. Res. (1977), 13(3), 355-61
 CODEN: MIVRA6
 DT Journal
 LA English
 CC 14-3 (Mammalian Pathological Biochemistry)
 Section cross-reference(s): 13
 AB To study the effect of prolonged elevation of plasma inorganic phosphate (Pi) on red cell metabolism and function, oxyhemoglobin dissocn. curves from zero to full satn. were performed on whole blood from insulin-treated, nonacidotic diabetics and healthy volunteers following oral administration of disodium ethane-1-hydroxy-1,1-diphosphonate (EHDP) (20 mg kg-1 day-1) or placebo for 28 days. EHDP increased mean Pi and pO2 at 50% O2 satn. (P50). P1 and P50 were correlated in both diabetics and controls. Mean P50 in diabetics was lower than normal in spite of normal red cell 2,3-diphosphoglycerate. 2,3-Diphosphoglycerate increased when the diabetics were on EHDP, while no changes occurred in Hb concn., O satn., or blood pH. The study emphasizes the importance of Pi on red cell function and indicates that an elevation of Pi tends to counteract the defect in oxygen-release capacity of the red cells in diabetic subjects.
 ST Hb oxygen affinity diabetes; phosphate Hb oxygen affinity
 IT **Diabetes mellitus**
 (hemoglobin oxygen binding in, phosphate of blood in relation to)
 IT Hemoglobins
 RL: BIOL (Biological study)
 (oxygen binding of, phosphate of blood in relation to)
 IT Blood
 (phosphate of, hemoglobin oxygen affinity in relation to)
 IT 7782-44-7, biological studies
 RL: BIOL (Biological study)
 (hemoglobin binding of, phosphate of blood in relation to)
 IT 14265-44-2, biological studies
 RL: BIOL (Biological study)
 (of blood, hemoglobin oxygen binding in relation to)
 IT **7414-83-7**
 RL: BIOL (Biological study)
 (phosphate of blood in response to, hemoglobin oxygen affinity in relation to)
 IT **7414-83-7**
 RL: BIOL (Biological study)
 (phosphate of blood in response to, hemoglobin oxygen affinity in relation to)
 RN 7414-83-7 HCAPLUS
 CN Phosphonic acid, (1-hydroxyethylidene)bis-, disodium salt (9CI) (CA INDEX NAME)



● 2 Na

=> fil reg

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STRUCTURE FILE UPDATES: 3 APR 2001 HIGHEST RN 329897-04-3
DICTIONARY FILE UPDATES: 3 APR 2001 HIGHEST RN 329897-04-3

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conducting SmartSELECT searches.

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for details.

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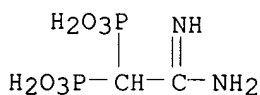
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33	RN	151425-93-3	REGISTRY
34	RN	151425-92-2	REGISTRY
35	RN	151425-91-1	REGISTRY
36	RN	151425-90-0	REGISTRY
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40	RN	124351-85-5	REGISTRY
41	RN	121268-17-5	REGISTRY
42	RN	118072-93-8	REGISTRY
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44	RN	105462-24-6	REGISTRY
45	RN	105462-23-5	REGISTRY
46	RN	89987-06-4	REGISTRY

DR 96538-83-9
 47 RN 89130-99-4 REGISTRY
 48 RN 79778-41-9 REGISTRY
 49 RN 66376-36-1 REGISTRY
 50 RN 57248-88-1 REGISTRY
 51 RN 41003-10-5 REGISTRY
 52 RN 40391-99-9 REGISTRY
 53 RN 34393-98-1 REGISTRY
 54 RN 29712-28-5 REGISTRY
 55 RN 15468-10-7 REGISTRY
 56 RN 15049-85-1 REGISTRY
 57 RN 10596-23-3 REGISTRY
 DR 163706-60-3
 58 RN 7414-83-7 REGISTRY
 DR 187285-10-5
 59 RN 7292-42-4 REGISTRY
 DR 172664-67-4, 55916-39-7
 60 RN 2809-21-4 REGISTRY
 DR 129130-42-3, 51888-66-5, 66216-98-6, 85985-26-8, 86159-18-4, 100511-44-2,
 106908-76-3
 61 RN 1984-15-2 REGISTRY
 DR 63347-66-0
 62 RN 1660-94-2 REGISTRY

=> d ide can 1138 1 2 4 37-62

Samples from huts
1-62, L138

L138 ANSWER 1 OF 62 REGISTRY COPYRIGHT 2001 ACS
 RN 253265-92-8 REGISTRY
 IN Phosphonic acid, (2-amino-2-iminoethylidene)bis- (9CI) (CA INDEX NAME)
 FS 3D CONCORD
 MF C2 H8 N2 O6 P2
 SR CA
 LC STN Files: CA, CAPLUS, TOXLIT

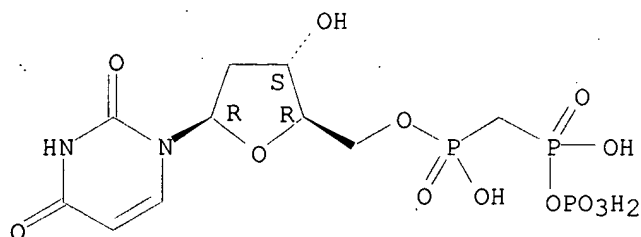


1 REFERENCES IN FILE CA (1967 TO DATE)
 1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:59143

L138 ANSWER 2 OF 62 REGISTRY COPYRIGHT 2001 ACS
 RN 170428-84-9 REGISTRY
 CN Uridine, 2'-deoxy-, 5'-[hydrogen [[hydroxy(phosphonooxy)phosphinyl]methyl]
 phosphonate] (9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C10 H17 N2 O13 P3
 SR CA
 LC STN Files: CA, CAPLUS, TOXLIT

Absolute stereochemistry.



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 123:330037

L138 ANSWER 4 OF 62 REGISTRY COPYRIGHT 2001 ACS

RN **151456-41-6** REGISTRY

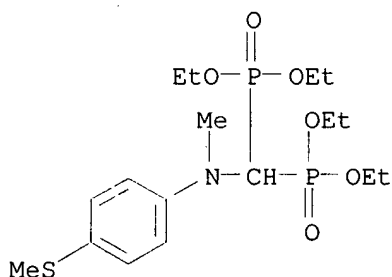
CN Phosphonic acid, [[methyl[4-(methylthio)phenyl]amino]methylene]bis-, tetraethyl ester (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C17 H31 N O6 P2 S

SR CA

LC STN Files: CA, CAPLUS, USPATFULL



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 120:8745

L138 ANSWER 37 OF 62 REGISTRY COPYRIGHT 2001 ACS

RN **138926-19-9** REGISTRY

CN Phosphonic acid, [1-hydroxy-3-(methylpentylamino)propylidene]bis-, monosodium salt, monohydrate (9CI) (CA INDEX NAME)

OTHER NAMES:

CN BM 21.0955Na.H2O

CN Ibandronate sodium monohydrate

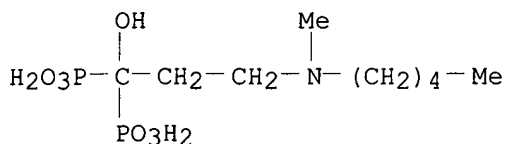
MF C9 H23 N O7 P2 . H2 O . Na

SR CAS Registry Services

LC STN Files: ADISINSIGHT, BIOTECHNO, CA, CAPLUS, DRUGPAT, DRUGUPDATES, EMBASE, MRCK*, SYNTHLINE, TOXLIT

(*File contains numerically searchable property data)

CRN (114084-78-5)



● Na

● H₂O

3 REFERENCES IN FILE CA (1967 TO DATE)

3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:284250

REFERENCE 2: 132:284249

REFERENCE 3: 132:69329

L138 ANSWER 38 OF 62 REGISTRY COPYRIGHT 2001 ACS

RN 138330-18-4 REGISTRY

CN Phosphonic acid, [(cycloheptylamino)methylene]bis-, disodium salt (9CI)
(CA INDEX NAME)

OTHER NAMES:

CN Incadronate

CN Incadronate disodium

CN YM 175

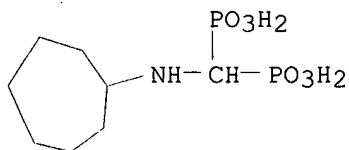
DR 183808-97-1

MF C8 H19 N O6 P2 . 2 Na

SR CA

LC STN Files: ADISINSIGHT, ANABSTR, BIOBUSINESS, BIOSIS, CA, CANCERLIT,
CAPLUS, CIN, DDFU, DRUGPAT, DRUGU, DRUGUPDATES, IPA, MEDLINE, MRCK*,
PHAR, PROMT, RTECS*, SYNTHLINE, TOXLINE, TOXLIT, USPATFULL
(*File contains numerically searchable property data)

CRN (124351-85-5)



● 2 Na

63 REFERENCES IN FILE CA (1967 TO DATE)

63 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:173008

REFERENCE 2: 134:36866

REFERENCE 3: 133:344627

REFERENCE 4: 133:313639

REFERENCE 5: 133:294826
 REFERENCE 6: 133:217722
 REFERENCE 7: 133:217721
 REFERENCE 8: 133:17634
 REFERENCE 9: 132:288773
 REFERENCE 10: 132:284250

L138 ANSWER 39 OF 62 REGISTRY COPYRIGHT 2001 ACS

RN 129318-43-0 REGISTRY

CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, monosodium salt (9CI)
 (CA INDEX NAME)

OTHER NAMES:

CN Alendronate sodium

CN Fosamax

CN MK 217

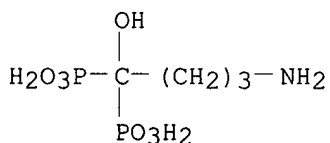
CN Monosodium alendronate

MF C4 H13 N O7 P2 . Na

SR CA

LC STN Files: ANABSTR, BIOBUSINESS, BIOSIS, CA, CAPLUS, CASREACT, CBNB,
 CEN, CHEMCATS, CIN, DIOGENES, DRUGPAT, DRUGUPDATES, IMSDIRECTORY, PHAR,
 PROMT, RTECS*, TOXLINE, TOXLIT, USPATFULL
 (*File contains numerically searchable property data)

CRN (66376-36-1)



● Na

66 REFERENCES IN FILE CA (1967 TO DATE)

2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

66 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:163171
 REFERENCE 2: 134:105948
 REFERENCE 3: 134:105846
 REFERENCE 4: 133:227815
 REFERENCE 5: 133:203006
 REFERENCE 6: 133:155456
 REFERENCE 7: 133:79271
 REFERENCE 8: 133:9079
 REFERENCE 9: 132:339369
 REFERENCE 10: 132:260684

L138 ANSWER 40 OF 62 REGISTRY COPYRIGHT 2001 ACS

RN 124351-85-5 REGISTRY

CN Phosphonic acid, [(cycloheptylamino)methylene]bis- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN Cimadronate

CN Cimadronic acid

CN Incadronic acid

CN [(Cycloheptylamino)methylene]bis(phosphonic acid)

CN [(Cycloheptylamino)methylene]diphosphonic acid

FS 3D CONCORD

MF C8 H19 N O6 P2

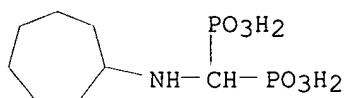
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SR CA

LC STN Files: ADISINSIGHT, BIOSIS, BIOTECHNO, CA, CAPLUS, DDFU, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, MRCK*, PROMT, SYNTHLINE, TOXLIT, USAN, USPATFULL

(*File contains numerically searchable property data)

Other Sources: WHO



39 REFERENCES IN FILE CA (1967 TO DATE)

4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

39 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:313639

REFERENCE 2: 133:276294

REFERENCE 3: 133:227815

REFERENCE 4: 133:203006

REFERENCE 5: 133:17634

REFERENCE 6: 133:9079

REFERENCE 7: 132:288795

REFERENCE 8: 132:288774

REFERENCE 9: 132:260710

REFERENCE 10: 132:156868

L138 ANSWER 41 OF 62 REGISTRY COPYRIGHT 2001 ACS

RN 121268-17-5 REGISTRY

CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, monosodium salt, trihydrate (9CI) (CA INDEX NAME)

OTHER NAMES:

CN Alendronate sodium hydrate

CN Sodium alendronate hydrate

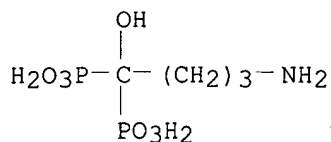
MF C4 H13 N O7 P2 . 3 H2 O . Na

SR US Adopted Names Council

LC STN Files: ADISINSIGHT, CA, CAPLUS, CBNB, CIN, DRUGPAT, DRUGUPDATES, IPA, MRCK*, PHAR, RTECS*, SYNTHLINE, TOXLINE, TOXLIT, USAN, USPATFULL

(*File contains numerically searchable property data)

CRN (66376-36-1)



● Na

● 3 H₂O

32 REFERENCES IN FILE CA (1967 TO DATE)

32 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:212746

REFERENCE 2: 134:91155

REFERENCE 3: 133:217721

REFERENCE 4: 133:9079

REFERENCE 5: 132:288773

REFERENCE 6: 132:199040

REFERENCE 7: 132:156868

REFERENCE 8: 132:69329

REFERENCE 9: 132:69328

REFERENCE 10: 132:69327

L138 ANSWER 42 OF 62 REGISTRY COPYRIGHT 2001 ACS

RN 118072-93-8 REGISTRY

CN Phosphonic acid, [1-hydroxy-2-(1H-imidazol-1-yl)ethylidene]bis- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN (1-Hydroxy-2-imidazol-1-ylethylidene)diphosphonic acid

CN CGP 42446

CN Zoledronate

CN Zoledronic acid

FS 3D CONCORD

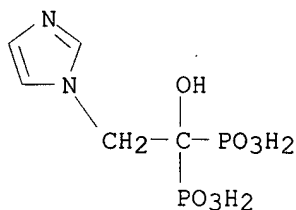
MF C5 H10 N2 O7 P2

CI COM

SR CA

LC STN Files: ADISINSIGHT, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CEN, CIN, DDFU, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, MEDLINE, MRCK*, PHAR, PROMT, SYNTHLINE, TOXLIT, USPATFULL
(*File contains numerically searchable property data)

Other Sources: WHO



71 REFERENCES IN FILE CA (1967 TO DATE)

7 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

72 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:173066

REFERENCE 2: 134:95352

REFERENCE 3: 134:36976

REFERENCE 4: 134:524

REFERENCE 5: 133:344627

REFERENCE 6: 133:313639

REFERENCE 7: 133:286495

REFERENCE 8: 133:252050

REFERENCE 9: 133:252041

REFERENCE 10: 133:246924

L138 ANSWER 43 OF 62 REGISTRY COPYRIGHT 2001 ACS

RN **114084-78-5** REGISTRY

CN Phosphonic acid, [1-hydroxy-3-(methylpentylamino)propylidene]bis- (9CI)
(CA INDEX NAME)

OTHER NAMES:

CN Ibandronate

CN Ibandronic acid

CN [1-Hydroxy-3-(methylpentylamino)propylidene]diphosphonic acid

FS 3D CONCORD

MF C9 H23 N O7 P2

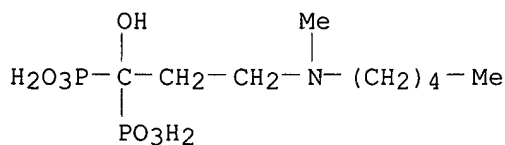
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SR CA

LC STN Files: ADISINSIGHT, ANABSTR, BIOSIS, BIOTECHNO, CA, CANCERLIT,
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EMBASE, IPA, MEDLINE, MRCK*, PHAR, PROMT, SYNTHLINE, TOXLINE, TOXLIT,
USAN, USPATFULL

(*File contains numerically searchable property data)

Other Sources: WHO



118 REFERENCES IN FILE CA (1967 TO DATE)

10 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

118 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:212746
REFERENCE 2: 134:125911
REFERENCE 3: 134:91155
REFERENCE 4: 134:36976
REFERENCE 5: 134:524
REFERENCE 6: 133:344627
REFERENCE 7: 133:313639
REFERENCE 8: 133:290623
REFERENCE 9: 133:276294
REFERENCE 10: 133:252050

L138 ANSWER 44 OF 62 REGISTRY COPYRIGHT 2001 ACS

RN 105462-24-6 REGISTRY

CN Phosphonic acid, [1-hydroxy-2-(3-pyridinyl)ethylidene]bis- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN NE 58019

CN Residronate

CN Risedronic acid

FS 3D CONCORD

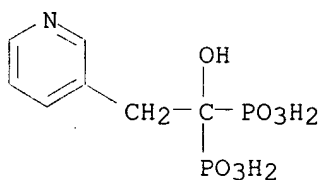
MF C7 H11 N O7 P2

CI COM

SR CA

LC STN Files: ADISINSIGHT, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, DDFU, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IPA, MEDLINE, MRCK*, PROMT, SYNTHLINE, TOXLINE, TOXLIT, USAN, USPATFULL
(*File contains numerically searchable property data)

Other Sources: WHO



167 REFERENCES IN FILE CA (1967 TO DATE)

12 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

167 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:212746
REFERENCE 2: 134:198075
REFERENCE 3: 134:178396
REFERENCE 4: 134:172899
REFERENCE 5: 134:163107
REFERENCE 6: 134:157507
REFERENCE 7: 134:125911

REFERENCE 8: 134:125893

REFERENCE 9: 134:91155

REFERENCE 10: 134:36976

L138 ANSWER 45 OF 62 REGISTRY COPYRIGHT 2001 ACS

RN 105462-23-5 REGISTRY

CN Phosphonic acid, [1-hydroxy-2-(2-pyridinyl)ethylidene]bis- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN NE 58018

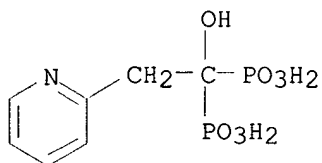
FS 3D CONCORD

MF C7 H11 N O7 P2

CI COM

SR CA

LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL



16 REFERENCES IN FILE CA (1967 TO DATE)

3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

16 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:252050

REFERENCE 2: 132:59143

REFERENCE 3: 130:162737

REFERENCE 4: 130:119056

REFERENCE 5: 125:316225

REFERENCE 6: 124:45749

REFERENCE 7: 122:322504

REFERENCE 8: 122:123154

REFERENCE 9: 121:245126

REFERENCE 10: 121:195927

L138 ANSWER 46 OF 62 REGISTRY COPYRIGHT 2001 ACS

RN 89987-06-4 REGISTRY

CN Phosphonic acid, [[(4-chlorophenyl)thio]methylene]bis- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN SR 41319

CN Tiludronate

CN Tiludronic acid

FS 3D CONCORD

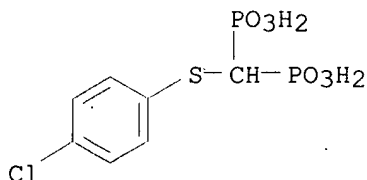
DR 96538-83-9

MF C7 H9 Cl O6 P2 S

CI COM

LC STN Files: ADISINSIGHT, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, DDFU, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IPA, MEDLINE, MRCK*, PHAR, PROMT, SYNTHLINE, TOXLINE, TOXLIT, USAN, USPATFULL

(*File contains numerically searchable property data)
Other Sources: WHO



106 REFERENCES IN FILE CA (1967 TO DATE)
8 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
106 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:198075

REFERENCE 2: 134:51352

REFERENCE 3: 134:36976

REFERENCE 4: 134:524

REFERENCE 5: 133:359206

REFERENCE 6: 133:344627

REFERENCE 7: 133:313639

REFERENCE 8: 133:252050

REFERENCE 9: 133:252041

REFERENCE 10: 133:227711

L138 ANSWER 47 OF 62 REGISTRY COPYRIGHT 2001 ACS

RN **89130-99-4** REGISTRY

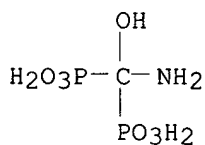
CN Phosphonic acid, (aminohydroxymethylene)bis- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C H7 N O7 P2

CI COM

LC STN Files: CA, CAPLUS, TOXLIT



3 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:59143

REFERENCE 2: 112:207764

REFERENCE 3: 100:109162

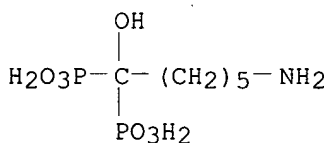
L138 ANSWER 48 OF 62 REGISTRY COPYRIGHT 2001 ACS

RN **79778-41-9** REGISTRY

CN Phosphonic acid, (6-amino-1-hydroxyhexylidene)bis- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 6-Amino-1-hydroxyhexane-1,1-diphosphonic acid
 CN 6-Amino-1-hydroxyhexylidene-1,1-bis(phosphonic acid)
 CN 6-Amino-1-hydroxyhexylidenediphosphonic acid
 CN Neridronate
 CN Neridronic acid
 FS 3D CONCORD
 MF C6 H17 N O7 P2
 CI COM
 LC STN Files: ADISINSIGHT, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, DRUGNL, DRUGUPDATES, EMBASE, MEDLINE, PHAR, PROMT, RTECS*, TOXLINE, TOXLIT, USAN, USPATFULL
 (*File contains numerically searchable property data)
 Other Sources: WHO



90 REFERENCES IN FILE CA (1967 TO DATE)
 6 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
 90 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:172899
 REFERENCE 2: 134:524
 REFERENCE 3: 133:344627
 REFERENCE 4: 133:313639
 REFERENCE 5: 133:252050
 REFERENCE 6: 133:252041
 REFERENCE 7: 133:217722
 REFERENCE 8: 133:217721
 REFERENCE 9: 133:203006
 REFERENCE 10: 133:9079

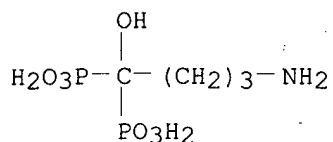
L138 ANSWER 49 OF 62 REGISTRY COPYRIGHT 2001 ACS

RN 66376-36-1 REGISTRY

CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 4-Amino-1-hydroxybutane-1,1-diphosphonate
 CN 4-Amino-1-hydroxybutane-1,1-diphosphonic acid
 CN 4-Amino-1-hydroxybutane-1,1-diylldiphosphonic acid
 CN 4-Amino-1-hydroxybutylidene-1,1-bis(phosphonic acid)
 CN Alendronate
 CN Alendronic acid
 FS 3D CONCORD
 MF C4 H13 N O7 P2
 CI COM
 LC STN Files: ADISINSIGHT, AGRICOLA, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CHEMCATS, CIN, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IPA, MEDLINE, MRCK*, PROMT, RTECS*, SYNTHLINE, TOXLINE, TOXLIT, USAN, USPATFULL
 (*File contains numerically searchable property data)
 Other Sources: WHO



496 REFERENCES IN FILE CA (1967 TO DATE)

21 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

497 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:212746

REFERENCE 2: 134:205856

REFERENCE 3: 134:198753

REFERENCE 4: 134:198075

REFERENCE 5: 134:188046

REFERENCE 6: 134:178396

REFERENCE 7: 134:172899

REFERENCE 8: 134:163171

REFERENCE 9: 134:157508

REFERENCE 10: 134:157507

L138 ANSWER 50 OF 62 REGISTRY COPYRIGHT 2001 ACS

RN 57248-88-1 REGISTRY

CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis-, disodium salt (9CI)
(CA INDEX NAME)

OTHER NAMES:

CN 3-Amino-1-hydroxypropane-1,1-diphosphonic acid disodium salt

CN APD

CN Aredia

CN CGP 23339A

CN Disodium 3-amino-1-hydroxypropane-1,1-diphosphonate

CN Disodium pamidronate

CN Pamidronate disodium

MF C3 H11 N O7 P2 . 2 Na

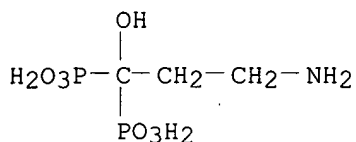
CI COM

LC STN Files: ADISINSIGHT, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA,
CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CIN, DIOGENES, DRUGPAT,
DRUGUPDATES, EMBASE, IFICDB, IFIPAT, IFIUDB, IMSDIRECTORY, MEDLINE,
MRCK*, PHAR, PROMT, RTECS*, SYNTHLINE, TOXLINE, TOXLIT, USPATFULL
(*File contains numerically searchable property data)

Other Sources: EINECS**

(**Enter CHEMLIST File for up-to-date regulatory information)

CRN (40391-99-9)



● 2 Na

67 REFERENCES IN FILE CA (1967 TO DATE)

67 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:198075

REFERENCE 2: 134:524

REFERENCE 3: 133:203183

REFERENCE 4: 133:183064

REFERENCE 5: 133:150625

REFERENCE 6: 133:34404

REFERENCE 7: 132:343276

REFERENCE 8: 132:260709

REFERENCE 9: 132:69329

REFERENCE 10: 132:61054

L138 ANSWER 51 OF 62 REGISTRY COPYRIGHT 2001 ACS

RN 41003-10-5 REGISTRY

CN Phosphonic acid, (2-amino-1-hydroxyethylidene)bis- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 2-Amino-1-hydroxyethane-1,1-diphosphonic acid

CN 2-Amino-1-hydroxyethylene-1,1-bisphosphonic acid

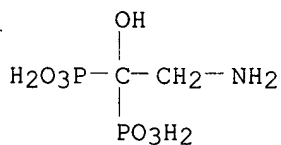
CN Ethane-1-hydroxy-2-amino-1,1-diphosphonic acid

FS 3D CONCORD

MF C2 H9 N O7 P2

CI COM

LC STN Files: CA, CAPLUS, IFICDB, IFIPAT, IFIUDB, TOXLIT, USPATFULL



18 REFERENCES IN FILE CA (1967 TO DATE)

3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

18 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:17535

REFERENCE 2: 132:59143

REFERENCE 3: 130:322256

REFERENCE 4: 130:38467

REFERENCE 5: 128:88965
 REFERENCE 6: 123:265312
 REFERENCE 7: 113:231496
 REFERENCE 8: 106:5628
 REFERENCE 9: 101:97713
 REFERENCE 10: 101:78908

L138 ANSWER 52 OF 62 REGISTRY COPYRIGHT 2001 ACS

RN 40391-99-9 REGISTRY

CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN (.alpha.-Hydroxy-.gamma.-aminopropylidene)diphosphonic acid

CN (3-Amino-1-hydroxypropylidene)-1,1-bisphosponate

CN 3-Amino-1-hydroxypropane-1,1-diphosphonic acid

CN 3-Amino-1-hydroxypropylidenediphosphonic acid

CN Amidronic acid

CN Pamidronic acid

CN Propane-1-hydroxy-3-amino-1,1-diphosphonic acid

FS 3D CONCORD

MF C3 H11 N O7 P2

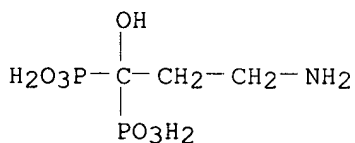
CI COM

LC STN Files: ADISINSIGHT, AIDSLINE, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CHEMCATS, CHEMINFORMRX, CHEMLIST, DDFU, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, SPECINFO, SYNTHLINE, TOXLINE, TOXLIT, USAN, USPATFULL, VETU

(*File contains numerically searchable property data)

Other Sources: EINECS**, WHO

(**Enter CHEMLIST File for up-to-date regulatory information)



465 REFERENCES IN FILE CA (1967 TO DATE)

23 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

466 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:198753
 REFERENCE 2: 134:178396
 REFERENCE 3: 134:173066
 REFERENCE 4: 134:172899
 REFERENCE 5: 134:95352
 REFERENCE 6: 134:91155
 REFERENCE 7: 134:80723
 REFERENCE 8: 134:36976
 REFERENCE 9: 134:32972

REFERENCE 10: 134:17535

L138 ANSWER 53 OF 62 REGISTRY COPYRIGHT 2001 ACS

RN 34393-98-1 REGISTRY

CN Phosphonic acid, (cyclohexylhydroxymethylene)bis- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Phosphonic acid, (cyclohexylhydroxymethylene)di- (8CI)

OTHER NAMES:

CN Cyclohexylhydroxymethanediphosphonate

CN Cyclohexylhydroxymethanediphosphonic acid

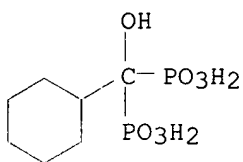
CN Methanecyclohexylhydroxydiphosphonic acid

FS 3D CONCORD

MF C7 H16 O7 P2

CI COM

LC STN Files: CA, CAPLUS, IFICDB, IFIPAT, IFIUDB, TOXLIT, USPATFULL



9 REFERENCES IN FILE CA (1967 TO DATE)

9 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 107:240873

REFERENCE 2: 95:90816

REFERENCE 3: 92:164036

REFERENCE 4: 90:61236

REFERENCE 5: 87:127290

REFERENCE 6: 86:183158

REFERENCE 7: 83:172652

REFERENCE 8: 80:74342

REFERENCE 9: 75:52779

L138 ANSWER 54 OF 62 REGISTRY COPYRIGHT 2001 ACS

RN 29712-28-5 REGISTRY

CN Phosphonic acid, (aminomethylene)bis- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Phosphonic acid, (aminomethylene)di- (8CI)

OTHER NAMES:

CN (Aminomethylene)di[phosphonic acid]

CN Aminomethanebis[phosphonic acid]

CN Aminomethanediphosphonic acid

CN Aminomethylenebis[phosphonic acid]

CN Aminomethylenediphosphonate

CN Methaneaminodiphosphonic acid

FS 3D CONCORD

MF C H7 N O6 P2

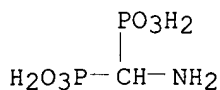
CI COM

LC STN Files: AGRICOLA, BEILSTEIN*, BIOSIS, CA, CAPLUS, CASREACT, CHEMCATS, CHEMINFORMRX, CHEMLIST, IFICDB, IFIPAT, IFIUDB, TOXLINE, TOXLIT, USPATFULL

(*File contains numerically searchable property data)

Other Sources: EINECS**

(**Enter CHEMLIST File for up-to-date regulatory information)



86 REFERENCES IN FILE CA (1967 TO DATE)
13 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
86 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:67398
REFERENCE 2: 133:325546
REFERENCE 3: 133:164174
REFERENCE 4: 133:146717
REFERENCE 5: 132:298659
REFERENCE 6: 132:51339
REFERENCE 7: 130:322256
REFERENCE 8: 130:38467
REFERENCE 9: 129:132964
REFERENCE 10: 128:149201

L138 ANSWER 55 OF 62 REGISTRY COPYRIGHT 2001 ACS

RN **15468-10-7** REGISTRY

CN Phosphonic acid, (hydroxymethylene)bis- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Phosphonic acid, (hydroxymethylene)di- (8CI)

OTHER NAMES:

CN 1-Hydroxy-1,1-diphosphonmethane

CN 1-Hydroxymethylene-1,1-bisphosphonic acid

CN HMDP

CN Hydroxymethanediphosphonic acid

CN Hydroxymethylenediphosphonate

CN Hydroxymethylenediphosphonic acid

CN MHDP

CN Oxidronic acid

FS 3D CONCORD

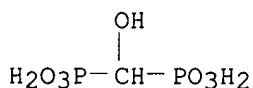
MF C H6 O7 P2

CI COM

LC STN Files: AGRICOLA, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, MEDLINE, MRCK*, PHAR, PROMT, TOXLINE, TOXLIT, USAN, USPATFULL

(*File contains numerically searchable property data)

Other Sources: WHO



106 REFERENCES IN FILE CA (1967 TO DATE)
32 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
106 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:178578

REFERENCE 2: 134:178396
 REFERENCE 3: 134:168857
 REFERENCE 4: 134:61555
 REFERENCE 5: 133:310142
 REFERENCE 6: 133:309791
 REFERENCE 7: 133:249161
 REFERENCE 8: 132:83729
 REFERENCE 9: 131:25531
 REFERENCE 10: 130:322256

L138 ANSWER 56 OF 62 REGISTRY COPYRIGHT 2001 ACS

RN 15049-85-1 REGISTRY

CN Phosphonic acid, (1-aminoethylidene)bis- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Phosphonic acid, (1-aminoethylidene)di- (6CI, 7CI, 8CI)

OTHER NAMES:

CN .alpha.-Aminoethane-.alpha.,.alpha.-diphosphonic acid

CN 1-(Aminoethylidene)-1,1-diphosphonic acid

CN 1-Amino-1,1-ethanediphosphonic acid

CN 1-Amino-1,1-ethanediylbis(phosphonic acid)

CN 1-Aminoethane-1,1-phosphonic acid

CN 1-Aminoethylidene-1,1-bisphosphonic acid

CN 1-Aminoethylidenediphosphonic acid

CN AEDP

CN Ethane-1-amino-1,1-diphosphonic acid

FS 3D CONCORD

MF C2 H9 N O6 P2

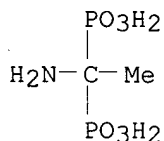
CI COM

LC STN Files: BEILSTEIN*, BIOSIS, CA, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMLIST, GMELIN*, IFICDB, IFIPAT, IFIUDB, TOXLIT, USPATFULL

(*File contains numerically searchable property data)

Other Sources: EINECS**

(**Enter CHEMLIST File for up-to-date regulatory information)



135 REFERENCES IN FILE CA (1967 TO DATE)

14 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

136 REFERENCES IN FILE CAPLUS (1967 TO DATE)

2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 134:125543
 REFERENCE 2: 134:58653
 REFERENCE 3: 134:38913
 REFERENCE 4: 133:344627
 REFERENCE 5: 132:51339

REFERENCE 6: 131:45405
REFERENCE 7: 130:349087
REFERENCE 8: 130:322256
REFERENCE 9: 130:121497
REFERENCE 10: 129:127186

L138 ANSWER 57 OF 62 REGISTRY COPYRIGHT 2001 ACS

RN 10596-23-3 REGISTRY

CN Phosphonic acid, (dichloromethylene)bis- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Phosphonic acid, (dichloromethylene)di- (8CI)

OTHER NAMES:

CN (Dichloromethylene)bis[phosphonic acid]

CN Clodronic acid

CN Dichloromethylenediphosphonic acid

CN Methanedichlorodiphosphonic acid

FS 3D CONCORD

DR 163706-60-3

MF C H4 Cl2 O6 P2

CI COM

LC STN Files: ADISINSIGHT, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS,
BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CHEMLIST, DDFU, DRUGNL, DRUGU,
DRUGUPDATES, EMBASE, IFICDB, IFIPAT, IFIUDb, IPA, MEDLINE, MRCK*, PHAR,
RTECS*, SYNTHLINE, TOXLINE, TOXLIT, USAN, USPATFULL

(*File contains numerically searchable property data)

Other Sources: EINECS**, WHO

(**Enter CHEMLIST File for up-to-date regulatory information)

H₂O₃P-CCl₂-PO₃H₂

545 REFERENCES IN FILE CA (1967 TO DATE)

27 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

545 REFERENCES IN FILE CAPLUS (1967 TO DATE)

1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 134:198075
REFERENCE 2: 134:125911
REFERENCE 3: 134:112037
REFERENCE 4: 134:95438
REFERENCE 5: 134:36976
REFERENCE 6: 134:36654
REFERENCE 7: 134:16484
REFERENCE 8: 134:13192
REFERENCE 9: 134:13035
REFERENCE 10: 134:524

L138 ANSWER 58 OF 62 REGISTRY COPYRIGHT 2001 ACS

RN 7414-83-7 REGISTRY

CN Phosphonic acid, (1-hydroxyethylidene)bis-, disodium salt (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Phosphonic acid, (1-hydroxyethylidene)di-, disodium salt (8CI)

OTHER NAMES:

CN 1-Hydroxyethane-1,1-diphosphonic acid disodium salt

CN BA 49280E

CN Didronel

CN Didronel R

CN Disodium (1-hydroxyethylidene)-1,1-bisphosphonate

CN Disodium (1-hydroxyethylidene)-1,1-diphosphonate

CN Disodium 1-hydroxy-1,1-ethanediphosphonate

CN Disodium 1-hydroxyethane-1-diphosphonate

CN Disodium 1-hydroxyethanediphosphonate

CN Disodium 1-hydroxyethylidenediphosphonate

CN Disodium ethane-1-hydroxy-1,1-diphosphonate

CN Disodium ethane-1-hydroxy-1,1-diphosphonic acid

CN Disodium ethane-1-hydroxy-1-diphosphonate

CN Disodium ethanol-1,1-diphosphonate

CN Disodium ethydrionate

CN Disodium etidronate

CN Etidronate disodium

CN Fostex NZ 2

CN Ostedron

CN Sequion 10Na2

CN Sodium ethane-1-hydroxy-1,1-diphosphonate

CN Sodium ethidronate

CN Sodium ethydrionate

CN Sodium etidronate

CN Turpinal 2NZ

DR 187285-10-5

MF C2 H8 O7 P2 . 2 Na

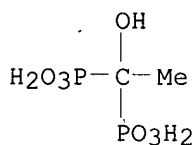
CI COM

LC STN Files: AGRICOLA, AIDSLINE, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CBNB, CHEMCATS, CHEMLIST, CIN, DIOGENES, EMBASE, IFICDB, IFIPAT, IFIUDB, IMSDIRECTORY, IPA, MEDLINE, MRCK*, NIOSHTIC, PHAR, PROMT, RTECS*, TOXLINE, TOXLIT, USAN, USPATFULL
(*File contains numerically searchable property data)

Other Sources: EINECS**, NDSL**, TSCA**

(**Enter CHEMLIST File for up-to-date regulatory information)

CRN (2809-21-4)



● 2 Na

305 REFERENCES IN FILE CA (1967 TO DATE)

8 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

305 REFERENCES IN FILE CAPLUS (1967 TO DATE)

1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 134:46896

REFERENCE 2: 134:44099

REFERENCE 3: 134:21496

REFERENCE 4: 133:183064

REFERENCE 5: 133:58455

REFERENCE 6: 133:47778

REFERENCE 7: 132:293042

REFERENCE 8: 132:260709

REFERENCE 9: 132:83650

REFERENCE 10: 132:59008

L138 ANSWER 59 OF 62 REGISTRY COPYRIGHT 2001 ACS

RN 7292-42-4 REGISTRY

CN Adenosine, 5'-[hydrogen [[hydroxy(phosphonooxy)phosphinyl]methyl]phosphonate] (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Adenosine, 5'-(trihydrogen methylenediphosphonate), monoanhydride with phosphoric acid (8CI)

CN Adenosine, 5'-methylenediphosphonate, anhydride with H3PO4 (7CI)

OTHER NAMES:

CN (.alpha.,.beta.-Methylene)adenosine 5'-triphosphate

CN (.alpha.,.beta.-Methylene)adenosine triphosphate

CN .alpha.,.beta.-Methylene 5'-ATP

CN .alpha.,.beta.-Methylene-ATP

CN Adenosine 5'-(.alpha.,.beta.-methylenetriphosphate)

CN Adenosine 5'-(.alpha.,.beta.-methylenetriphosphonate)

CN Adenosine 5'-methylenediphosphono-P2-phosphate

CN ATP, .alpha.,.beta.-methylene-

FS STEREOSEARCH

DR 1:72664-67-4, 55916-39-7

MF C11 H18 N5 O12 P3

CI COM

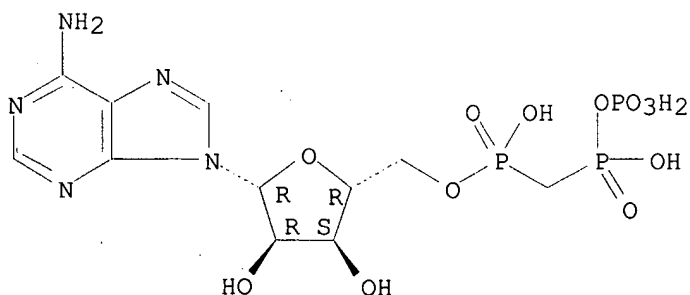
LC STN Files: BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CHEMCATS, CHEMLIST, CSCHEM, DDFU, DRUGU, EMBASE, IPA, MEDLINE, TOXLINE, TOXLIT, USPATFULL

(*File contains numerically searchable property data)

Other Sources: EINECS**

(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



651 REFERENCES IN FILE CA (1967 TO DATE)

3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

651 REFERENCES IN FILE CAPLUS (1967 TO DATE)

1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 134:188528

REFERENCE 2: 134:188497

REFERENCE 3: 134:188496

REFERENCE 4: 134:188494
REFERENCE 5: 134:188297
REFERENCE 6: 134:176060
REFERENCE 7: 134:173317
REFERENCE 8: 134:158009
REFERENCE 9: 134:110770
REFERENCE 10: 134:82686

L138 ANSWER 60 OF 62 REGISTRY COPYRIGHT 2001 ACS

RN 2809-21-4 REGISTRY

CN Phosphonic acid, (1-hydroxyethylidene)bis- (9CI) (CA INDEX NAME)

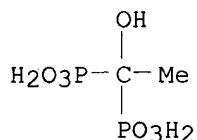
OTHER CA INDEX NAMES:

CN Phosphonic acid, (1-hydroxyethylidene)di- (8CI)

OTHER NAMES:

CN (1-Hydroxyethylidene)-1,1-bis(phosphonic acid)
CN (1-Hydroxyethylidene)-1,1-diphosphonic acid
CN (1-Hydroxyethylidene)bisphosphonic acid
CN (1-Hydroxyethylidene)diphosphonic acid
CN 1-Hydroxy-1,1-diphosphonoethane
CN 1-Hydroxyethane-1,1-bisphosphonic acid
CN 1-Hydroxyethane-1,1-diphosphonic acid
CN 1-Hydroxyethane-1,1-diylldiphosphonic acid
CN 1-Hydroxyethanediphosphonic acid
CN 1000SL
CN Acetodiphosphonic acid
CN Briquest ADPA 60A
CN Cublen K 60
CN Defloc EH 06
CN Dequest 16
CN Dequest 2010
CN Dequest 2010CS
CN Dequest 2015
CN Dequest Z 010
CN EHDP
CN Ethane-1-hydroxy-1,1-diphosphonic acid
CN Etidronic acid
CN Ferriox 115
CN Ferriox CY 115
CN Ferrofos 510
CN HDEPA
CN HEDP
CN Hydroxyethanediphosphonic acid
CN Ksidifon
CN Lonza 106
CN Masquol P 210
CN Mayoquest 1500
CN OEDF
CN OEDP
CN Oxyethylidenediphosphonic acid
CN RP 61
CN Sone 16
CN Tecquest 360
CN Terpil SL
CN Turpinal SL
CN Turpinal SLR
CN Wayplex
CN Xidiphone
CN Xydiphone
FS 3D CONCORD
DR 129130-42-3, 51888-66-5, 66216-98-6, 85985-26-8, 86159-18-4, 100511-44-2,

106908-76-3
 MF C2 H8 O7 P2
 CI COM
 LC STN Files: AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS,
 BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS,
 CHEMLIST, CIN, CSCHEM, DDFU, DETHERM*, DRUGNL, DRUGU, EMBASE, GMELIN*,
 HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, PHAR,
 PIRA, PROMT, RTECS*, TOXLINE, TOXLIT, USAN, USPATFULL, VETU
 (*File contains numerically searchable property data)
 Other Sources: DSL**, EINECS**, TSCA**, WHO
 (**Enter CHEMLIST File for up-to-date regulatory information)



3286 REFERENCES IN FILE CA (1967 TO DATE)
 398 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
 3288 REFERENCES IN FILE CAPLUS (1967 TO DATE)
 5 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 134:211055
 REFERENCE 2: 134:209763
 REFERENCE 3: 134:209755
 REFERENCE 4: 134:209747
 REFERENCE 5: 134:206810
 REFERENCE 6: 134:204392
 REFERENCE 7: 134:198753
 REFERENCE 8: 134:197890
 REFERENCE 9: 134:196665
 REFERENCE 10: 134:194692

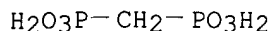
L138 ANSWER 61 OF 62 REGISTRY COPYRIGHT 2001 ACS
 RN 1984-15-2 REGISTRY
 CN Phosphonic acid, methylenebis- (9CI) (CA INDEX NAME)
 OTHER CA INDEX NAMES:
 CN Phosphonic acid, methylenedi- (6CI, 7CI, 8CI)
 OTHER NAMES:
 CN MDP
 CN Medronic acid
 CN Methanebisphosphonic acid
 CN Methanediphosphonic acid
 CN Methylene-1,1-bisphosphonic acid
 CN Methylenebis[phosphonic acid]
 CN Methylenediphosphonic acid
 FS 3D CONCORD
 DR 63347-66-0
 MF C H6 O6 P2
 CI COM
 LC STN Files: AGRICOLA, AIDSLINE, BEILSTEIN*, BIOBUSINESS, BIOSIS,
 BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CHEMCATS,
 CHEMINFORMRX, CHEMLIST, CSCHEM, DDFU, DRUGU, EMBASE, GMELIN*, IFICDB,
 IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, TOXLINE,

TOXLIT, USAN, USPATFULL

(*File contains numerically searchable property data)

Other Sources: EINECS**, WHO

(**Enter CHEMLIST File for up-to-date regulatory information)



702 REFERENCES IN FILE CA (1967 TO DATE)

353 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

705 REFERENCES IN FILE CAPLUS (1967 TO DATE)

13 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 134:187397

REFERENCE 2: 134:125543

REFERENCE 3: 134:117642

REFERENCE 4: 134:106509

REFERENCE 5: 134:105862

REFERENCE 6: 134:80108

REFERENCE 7: 134:68125

REFERENCE 8: 134:61555

REFERENCE 9: 134:53165

REFERENCE 10: 134:17535

L138 ANSWER 62 OF 62 REGISTRY COPYRIGHT 2001 ACS

RN 1660-94-2 REGISTRY

CN Phosphonic acid, methylenebis-, tetraethyl ester (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Phosphonic acid, methylenedi-, tetraethyl ester (6CI, 7CI, 8CI)

OTHER NAMES:

CN Bis(diethylphosphono)methane

CN Methanediphosphonic acid tetraethyl ester

CN Methylenebis(diethoxyphosphine oxide)

CN Methylenebis(diethyl phosphonate)

CN Methylenebis(phosphonic acid) tetraethyl ester

CN Methylenediphosphonic acid tetraethyl ester

CN Tetraethyl methylenebisphosphonate

CN Tetraethyl methylenediphosphonate

CN Tetraethyl methylenedibisphosphonate

FS 3D CONCORD

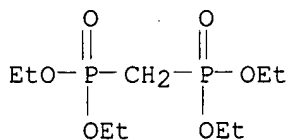
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LC STN Files: BEILSTEIN*, BIOSIS, CA, CAOLD, CAPLUS, CASREACT, CHEMCATS,
 CHEMINFORMRX, CHEMLIST, CSCHEM, IFICDB, IFIPAT, IFIUDB, RTECS*,
 SPECINFO, TOXLIT, USPATFULL

(*File contains numerically searchable property data)

Other Sources: EINECS**, NDSL**, TSCA**

(**Enter CHEMLIST File for up-to-date regulatory information)



308 REFERENCES IN FILE CA (1967 TO DATE)
4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
308 REFERENCES IN FILE CAPLUS (1967 TO DATE)
12 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

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REFERENCE 2: 134:131597
REFERENCE 3: 134:116015
REFERENCE 4: 133:281830
REFERENCE 5: 133:171382
REFERENCE 6: 133:150624
REFERENCE 7: 133:135358
REFERENCE 8: 133:120554
REFERENCE 9: 133:58868
REFERENCE 10: 132:347650

=> fil medline

FILE 'MEDLINE' ENTERED AT 11:16:57 ON 04 APR 2001

FILE LAST UPDATED: 22 MAR 2001 (20010322/UP). FILE COVERS 1958 TO DATE.

MEDLINE now contains new records from the former NLM HEALTH STAR database. These records have an Entry Date and Update Date of 20010223.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2001 vocabulary. Enter HELP THESAURUS for details.

The OLDMEDLINE file segment now contains data from 1958 through 1965. Enter HELP CONTENT for details.

Left, right, and simultaneous left and right truncation are available in the Basic Index. See HELP SFIELDS for details.

THIS FILE CONTAINS CAS REGISTRY NUMBERS FOR EASY AND ACCURATE SUBSTANCE IDENTIFICATION.

MEDLINE has been updated with new records for the 2001 production year (20010322/UP). NLM is still in the process of preparing data. Therefore, regular updates to the file are not in place. As soon as NLM makes the regular updates available, we will process the update.

=> d his 1139-

(FILE 'REGISTRY' ENTERED AT 11:02:57 ON 04 APR 2001)
SAV L138 KWON7199B/A

FILE 'REGISTRY' ENTERED AT 11:03:49 ON 04 APR 2001

FILE 'HCAPLUS' ENTERED AT 11:04:10 ON 04 APR 2001

FILE 'REGISTRY' ENTERED AT 11:05:11 ON 04 APR 2001

FILE 'MEDLINE' ENTERED AT 11:06:46 ON 04 APR 2001
L139 6159 S L6

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L140      742 S L11
L141      6887 S L139,L140
           E DIPHOSPHONATE/CT
           E E10+ALL
L142      6739 S E4+NT
           E DIPHOSPHONATE#/CN
L143      3464 S E4
L144      8339 S L141-L143
           E AUTOIMMUN/CT
L145      205946 S E17+NT
L146      3621 S E105+NT
L147      130 S L144 AND L145,L146
L148      104 S L147 AND PY<=1998
L149      25 S L148 NOT AB/FA
L150      2422 S ((DIPHOSPHONATES+NT) (L)TU.)/CT
L151      6 S L150 AND L149
L152      4 S L151 NOT PAGET/TI
L153      79 S L148 NOT L149
L154      13 S L150 AND L153
L155      66 S L153 NOT L154
L156      23 S L155 NOT TECHNETIUM TC 99M MEDRONATE/CT,CN
L157      13 S L156 NOT (99MTC OR TECHNETIUM)
L158      30 S L152,L154,L157

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FILE 'MEDLINE' ENTERED AT 11:16:57 ON 04 APR 2001

=> d all tot l158

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L158 ANSWER 1 OF 30 MEDLINE
AN 1999169424 MEDLINE
DN 99169424
TI Cyclical etidronate increases bone density in the spine and hip of
   postmenopausal women receiving long term corticosteroid treatment. A
   double blind, randomised placebo controlled study.
AU Geusens P; Dequeker J; Vanhoof J; Stalmans R; Boonen S; Joly J; Nijs J;
   Raus J
CS Instituut, Diepenbeek, Belgium.
SO ANNALS OF THE RHEUMATIC DISEASES, (1998 Dec) 57 (12) 724-7.
   Journal code: 62W. ISSN: 0003-4967.
CY ENGLAND: United Kingdom
DT (CLINICAL TRIAL)
   Journal; Article; (JOURNAL ARTICLE)
   (RANDOMIZED CONTROLLED TRIAL)
LA English
FS Priority Journals
EM 199905
EW 19990502
AB OBJECTIVE: To study the effect of cyclic etidronate in secondary
   prevention of corticosteroid induced osteoporosis. METHODS: A double
   blind, randomised placebo controlled study comparing cyclic etidronate and
   placebo during two years in 37 postmenopausal women receiving long term
   corticosteroid treatment, mainly for polymyalgia rheumatica (40% of the
   patients) and rheumatoid arthritis (30%). Bone density was measured in the
   lumbar spine, femoral neck, and femoral trochanter. RESULTS: After two
   years of treatment there was a significant difference between the groups
   in mean per cent change from baseline in bone density in the spine in
   favour of etidronate (p = 0.003). The estimated treatment difference (mean
   (SD)) was 9.3 (2.1)%. Etidronate increased bone density in the spine (4.9
   (2.1)%, p < 0.05) whereas the placebo group lost bone (-2.4 (1.6)%). At
   the femoral neck there was an estimated difference of 5.3 (2.6)% between
   the groups (etidronate: 3.6% (1.4)%, p < 0.05, placebo: -2.4 (2.1)%). The
   estimated difference at the trochanter was 8.2 (3.0) (etidronate: 9.0
   (1.5)%, p < 0.0001, placebo: 0.5 (2.3)%). No significant bone loss
   occurred in the hip in placebo treated patients. CONCLUSIONS: Cyclic
   etidronate is an effective treatment for postmenopausal women receiving

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corticosteroid treatment and is well tolerated.
 CT Check Tags: Female; Human; Support, Non-U.S. Gov't
 Aged
 Analysis of Variance
Arthritis, Rheumatoid: DT, drug therapy
 *Bone Density: DE, drug effects
 *Calcium: AD, administration & dosage
 Calcium: TU, therapeutic use
 Double-Blind Method
 Drug Administration Schedule
 *Etidronate Disodium: AD, administration & dosage
 Etidronate Disodium: TU, therapeutic use
 Femur Neck: PP, physiopathology
 *Glucocorticoids, Synthetic: AE, adverse effects
 Glucocorticoids, Synthetic: TU, therapeutic use
 Lumbar Vertebrae: PP, physiopathology
 Middle Age
 *Osteoporosis: CI, chemically induced
 *Osteoporosis: PC, prevention & control
 Polymyalgia Rheumatica: DT, drug therapy
 Postmenopause
 Statistics, Nonparametric
 RN **7414-83-7 (Etidronate Disodium); 7440-70-2 (Calcium)**
 CN 0 (Glucocorticoids, Synthetic)

L158 ANSWER 2 OF 30 MEDLINE

AN 1998430703 MEDLINE

DN 98430703

TI Immune invasion of the central nervous system parenchyma and experimental allergic encephalomyelitis, but not leukocyte extravasation from blood, are prevented in macrophage-depleted mice.

AU Tran E H; Hoekstra K; van Rooijen N; Dijkstra C D; Owens T

CS Montreal Neurological Institute, Department of Microbiology and Immunology, McGill University, Quebec, Canada.

SO JOURNAL OF IMMUNOLOGY, (1998 Oct 1) 161 (7) 3767-75.

Journal code: IFB. ISSN: 0022-1767.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals

EM 199812

AB Organ-specific autoimmune diseases are characterized by infiltrates, including T lymphocytes and activated macrophages. Macrophages and secondarily activated tissue resident counterparts can both present Ag to and contribute to cytokine secretion by T lymphocytes. We have previously shown a crucial role of peripheral macrophages in experimental allergic encephalomyelitis (EAE), a Th1-mediated demyelinating disease that serves as an animal model for multiple sclerosis (MS), by their depletion using mannosylated liposome-encapsulated dichloromethylene diphosphonate (Cl2MDP). Here we describe studies to investigate the mechanisms by which macrophages contribute to the lesion formation in EAE, by studying the effect of Cl2MDP-containing mannosylated liposomes (Cl2MDP-mnL) on adoptively transferred EAE in SJL/J mice. Adoptive transfer of EAE with myelin basic protein-reactive CD4+ T cells to SJL/J mice was abrogated by Cl2MDP-mnL treatment. CD4+ T cell and MHC II+ B220+ B cell extravasation from blood vessels and Th1 cytokine production were not inhibited. However, invasion of the central nervous system intraparenchymal tissues by lymphocytes, F4/80+, Mac-1+, and MOMA-1+ macrophages was almost completely blocked after treatment with Cl2MDP-mnL. Furthermore, in Cl2MDP-mnL-treated mice, the myelin sheaths appeared completely normal, whereas, in the control groups, marked demyelination occurred. Production of TNF-alpha and inducible nitric oxide synthase, both associated with macrophage/microglial activation, was inhibited. This intervention reveals a role for macrophages in regulating the invasion of autoreactive T cells and secondary glial recruitment that ordinarily lead to demyelinating pathology in EAE and multiple sclerosis.

CT Check Tags: Animal; Female; Support, Non-U.S. Gov't
 Acute Disease
 *Cell Movement: IM, immunology
 *Central Nervous System: IM, immunology
 Central Nervous System: PA, pathology
 Clodronic Acid: PD, pharmacology
 CD4-Positive T-Lymphocytes: PA, pathology
 Demyelinating Diseases: PA, pathology
 Demyelinating Diseases: PC, prevention & control
 *Encephalomyelitis, Experimental Autoimmune: IM, immunology
 Encephalomyelitis, Experimental Autoimmune: PA, pathology
 Encephalomyelitis, Experimental Autoimmune: PC, prevention & control
 Leukocytes, Mononuclear: DE, drug effects
 Leukocytes, Mononuclear: IM, immunology
 *Leukocytes, Mononuclear: PA, pathology
 Liposomes: ME, metabolism
 *Macrophages: IM, immunology
 Macrophages: PA, pathology
 Mannose: ME, metabolism
 Mice
 Mice, Inbred Strains
 Nitric-Oxide Synthase: AI, antagonists & inhibitors
 Nitric-Oxide Synthase: BI, biosynthesis
 Th1 Cells: DE, drug effects
 Th1 Cells: ME, metabolism
 Tumor Necrosis Factor: AI, antagonists & inhibitors
 Tumor Necrosis Factor: BI, biosynthesis
 RN 10596-23-3 (Clodronic Acid); 31103-86-3 (Mannose)
 CN EC 1.14.13.- (inducible nitric oxide synthase); EC 1.14.13.39
 (Nitric-Oxide Synthase); 0 (Liposomes); 0 (Tumor Necrosis Factor)

L158 ANSWER 3 OF 30 MEDLINE
 AN 1998377018 MEDLINE
 DN 98377018
 TI Abnormal bone remodelling in inflammatory arthritis.
 AU Bogoch E R; Moran E
 CS Orthopaedic Research Laboratory, St. Michael's Hospital, Wellesley Central
 Site, University of Toronto, Ont.
 SO CANADIAN JOURNAL OF SURGERY, (1998 Aug) 41 (4) 264-71. Ref: 21
 Journal code: CKJ. ISSN: 0008-428X.
 CY Canada
 DT Journal; Article; (JOURNAL ARTICLE)
 General Review; (REVIEW)
 (REVIEW, TUTORIAL)
 LA English
 FS Priority Journals
 EM 199811
 EW 19981102
 AB Osteopenia is responsible for substantial comorbidity in patients
 suffering from rheumatoid arthritis and is an important factor in the
 surgical management of joint disease. In animal models of bone loss
 stimulated by inflammatory arthritis, increased bone remodelling and
 altered microstructure of bone have been documented. The subchondral bone
 plate near the joint surface is narrow and perforated by vascular
 inflammatory invasion, and in the shaft the thin cortices are weakened by
 giant resorption defects. Biomechanical tests and a mathematical model of
 bone strength suggest that cortical defects, much larger than those found
 in normal osteonal remodelling, are principally responsible for the
 experimentally observed loss of strength. Similarly, these defects may
 explain the increased femoral fracture risk in rheumatoid arthritis. The
 osteoclast, the cell resorbing bone, is demonstrated in increased number
 and activity in rheumatoid arthritis and in animal models.
 Bisphosphonates, drugs that inhibit osteoclast function, have been shown
 experimentally to reduce both focal and generalized osteopenia and to
 prevent loss of bone strength. Bisphosphonates also protect articular

cartilage from damage characteristic of inflammatory arthritis. The mechanism of chondroprotection may be prevention of subchondral bone resorption by the osteoclast and also an altered distribution of bone marrow cells. Thus, bisphosphonates, currently in clinical use for other bone metabolic diseases, appear to have potential as prophylaxis and treatment for osteopenia and joint damage in inflammatory arthritis.

CT Check Tags: Animal; Human

Arthritis, Rheumatoid: PA, pathology

***Arthritis, Rheumatoid: PP, physiopathology**

Bone and Bones: PA, pathology

Bone Diseases: DT, drug therapy

Bone Diseases: PP, physiopathology

***Bone Remodeling**

Bone Remodeling: PH, physiology

Bone Resorption

Cartilage, Articular: DE, drug effects

Cartilage, Articular: PA, pathology

Diphosphonates: PD, pharmacology

Diphosphonates: TU, therapeutic use

Osteoblasts

Osteoclasts

CN **0 (Diphosphonates)**

L158 ANSWER 4 OF 30 MEDLINE

AN 1998279267 MEDLINE

DN 98279267

TI Differential effect of macrophage depletion on two forms of experimental uveitis evoked by pigment epithelial membrane protein (EAPU), and by melanin-protein (EMIU).

AU Broekhuysse R M; Huitinga I; Kuhlmann E D; Rooijen N V; Winkens H J

CS Institute of Ophthalmology, University of Nijmegen, The Netherlands.

SO EXPERIMENTAL EYE RESEARCH, (1997 Dec) 65 (6) 841-8.

Journal code: EPL. ISSN: 0014-4835..

CY ENGLAND: United Kingdom

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199808

EW 19980802

AB The purpose of the present study was to clinically and histologically investigate the influence of macrophage depletion on the development of experimental autoimmune pigment epithelial membrane protein-induced uveitis (EAPU), and experimental melanin-protein induced uveitis (EMIU) in the Lewis rat. EAPU is mainly characterized by pigment epitheliitis. Posterior mononuclear cell accumulations enclose and destroy the retinal pigment epithelium (RPE). In EMIU the inflammation is specifically localized in the uvea. EAPU was induced by immunization with RPE membrane protein, and EMIU was evoked by immunization with purified choroidal melanin. Systemic treatment with dichloromethylene diphosphonate (Cl2MDP)-containing liposomes just before the expected beginning of the clinical signs of EAPU (at day 7 and 9 after immunization) resulted in a considerable delay of the uveitis process. In the treated animals the typical plaque shaped cell accumulations (containing many macrophages) along the RPE were lacking. Two weeks after the treatment, severe rebound EAPU developed. Local treatment by subconjunctival liposome injections did not exert any effect on EAPU. In EMIU, macrophage depletion by systemic treatment did not noticeably influence the clinical and histological development of the inflammation. Systemic treatment at the peak stage of EAPU (at day 12 and 14 after immunization) resulted in the rapid disappearance of the clinical signs of uveitis. Vitreous and anterior chamber cells were virtually absent two days later. This situation remained unchanged until the experiment was terminated two weeks later. Already deposited cell accumulations along the RPE did not regress but stopped their progression. Hematogenous macrophages thus appear to play a crucial role in the development of EAPU but the effect of early macrophage depletion on EAPU appeared to be temporary due to blood repopulation. A

possible explanation for the differential influence of macrophage depletion on EAPU and EMIU is discussed, and is based on differences in immunopathogenesis.

CT Check Tags: Animal; Comparative Study; Female; Support, Non-U.S. Gov't
 *Autoimmune Diseases: IM, immunology
 Autoimmune Diseases: PA, pathology
 Autoimmune Diseases: PC, prevention & control
 Choroid: PA, pathology
 Clodronic Acid: TU, therapeutic use
 Disease Models, Animal
 *Eye Proteins: IM, immunology
 Immunization
 Liposomes
 Macrophages: DE, drug effects
 Macrophages: PA, pathology
 *Macrophages: PH, physiology
 *Melanins: IM, immunology
 Phagocytosis
 *Proteins: IM, immunology
 Rats
 Rats, Inbred Lew
 Retina: PA, pathology
 *Serpins: IM, immunology
 *Uveitis: IM, immunology
 Uveitis: PA, pathology
 Uveitis: PC, prevention & control
 RN 10596-23-3 (Clodronic Acid)
 CN 0 (pigment epithelium-derived factor); 0 (Eye Proteins); 0 (Liposomes); 0 (Melanins); 0 (Proteins); 0 (Serpins)

L158 ANSWER 5 OF 30 MEDLINE

AN 1998217257 MEDLINE

DN 98217257

TI An open study of pamidronate in the treatment of refractory ankylosing spondylitis.

AU Maksymowych W P; Jhangri G S; Leclercq S; Skeith K; Yan A; Russell A S

CS Department of Medicine, University of Alberta, Edmonton, Canada.

SO JOURNAL OF RHEUMATOLOGY, (1998 Apr) 25 (4) 714-7.

Journal code: JWX. ISSN: 0315-162X.

CY Canada

DT (CLINICAL TRIAL)

Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199808

EW 19980802

AB OBJECTIVE: Bisphosphonates inhibit the development of delayed type hypersensitivity chronic inflammation and suppress inflammation and cartilage/bone erosion in diverse murine arthritis models. We evaluated antiinflammatory properties of the bisphosphonate pamidronate in patients with ankylosing spondylitis (AS) refractory to nonsteroidal antiinflammatory drugs. METHODS: Patients included 14 men and 2 women. The first group of 8 patients (Group 1) received pamidronate as a 30 mg intravenous infusion once a month for 3 months, followed by a 60 mg dose once a month for an additional 3 months. Eight additional patients (Group 2) received only the 60 mg dose once a month for 3 months. Clinical assessments included the BASDAI (Bath AS Disease Activity Index), BASFI (Functional Index), and BASMI (Metrology Index), and laboratory assessments hemoglobin and erythrocyte sedimentation rate (ESR) at baseline and one month after final 60 mg dose of pamidronate. Mean BASDAI score at study entry was 6.7 for both groups. RESULTS: A significant improvement was observed in disease activity score in Group 1 after 6 monthly infusions of pamidronate (mean BASDAI 4.21; $p = 0.03$), in the BASMI score ($p = 0.01$), and the ESR ($p = 0.009$). A significant improvement in the BASMI was noted in Group 2 patients ($p = 0.007$) after 3 monthly infusions of pamidronate, but not in the BASDAI score (mean 5.01; $p =$

0.07) or the ESR ($p = 0.12$). CONCLUSION: Preliminary data suggest pamidronate may possess antiinflammatory activity in patients with AS, particularly with prolonged administration; this agent deserves further evaluation in a controlled trial.

CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't Adult

*Anti-Inflammatory Agents: TU, therapeutic use
Blood Sedimentation

*Diphosphonates: TU, therapeutic use
Middle Age

*Spondylitis, Ankylosing: DT, drug therapy
Treatment Outcome

RN 40391-99-9 (amidronate)

CN 0 (Anti-Inflammatory Agents); 0 (Diphosphonates)

L158 ANSWER 6 OF 30 MEDLINE

AN 1998070002 MEDLINE

DN 98070002

TI The ineffectiveness of cyclical oral clodronate on bone mineral density in glucocorticoid-treated patients with giant-cell arteritis.

AU Nordborg E; Schaufelberger C; Andersson R; Bosaeus I; Bengtsson B A

CS Division of Rheumatology, Sahlgrenska University Hospital, Goteborg, Sweden.

SO JOURNAL OF INTERNAL MEDICINE, (1997 Nov) 242 (5) 367-71.

Journal code: I2G. ISSN: 0954-6820.

CY ENGLAND: United Kingdom

DT (CLINICAL TRIAL)

(CONTROLLED CLINICAL TRIAL)

Journal; Article; (JOURNAL ARTICLE)

(RANDOMIZED CONTROLLED TRIAL)

LA English

FS Priority Journals; Cancer Journals

EM 199803

AB OBJECTIVES AND DESIGN: The aim of the present study was to determine whether cyclic oral administration of clodronate, a bisphosphonate, every second month prevents rapid bone loss during the first year of glucocorticoid treatment in patients with giant-cell arteritis (GCA). The trial was designed as a prospective double blind study, assessing total body mineral content (BMC) and bone mineral density (BMD) using DXA technique. Supplementation of calcium was given to both groups of patients. SETTING: The outpatient clinics of the rheumatic and infectious diseases of Sahlgren University Hospital of the city of Goteborg on the west coast of Sweden. SUBJECTS: Twenty-seven patients with confirmed GCA were consecutively included during a 15-month period. RESULTS: An early influence on bone turnover was found with a temporary decrease in BMC after six months of glucocorticoid treatment, which was normalized after 12 months in both study groups. No significant differences between the patients given clodronate and calcium and the controls, who got supplementation with calcium alone, was observed at any assessment point. However, there was a significant and prolonged depression of the osteocalcin levels in the clodronate-treated patients. CONCLUSIONS: Oral administration of clodronate in a moderately high dose given cyclically every other month had no additive effect on BMD compared with calcium supplementation alone during the first year of glucocorticoid treatment. A larger material might have revealed some differences between the categories. In most patients with GCA, however, the BMD seems to recover after one year of glucocorticoid treatment, provided there is good control of the inflammation and patients are kept physically active. It needs to be elucidated whether there are subsets of patients who might benefit from bone sparing agents: women near menopause with a high turnover rate of bone, individuals who have low BMD from the start of glucocorticoid treatment or patients requiring high doses of glucocorticoids during a long period of time.

CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't
Administration, Oral
Aged

Aged, 80 and over
 *Bone Density: DE, drug effects
 *Clodronic Acid: PD, pharmacology
 Double-Blind Method
 Drug Administration Schedule
 *Glucocorticoids: TU, therapeutic use
 Middle Age
 Prospective Studies
 *Temporal Arteritis: DT, drug therapy
 *Temporal Arteritis: PP, physiopathology
 Treatment Outcome

RN 10596-23-3 (Clodronic Acid)
 CN 0 (Glucocorticoids)

L158 ANSWER 7 OF 30 MEDLINE

AN 1998054043 MEDLINE

DN 98054043

TI Myositis ossificans complicating severe Guillain-Barre syndrome.

AU Hung J C; Appleton R E; Abernethy L

CS Department of Neurology, Royal Liverpool Children's Hospital, Alder Hey, UK.

SO DEVELOPMENTAL MEDICINE AND CHILD NEUROLOGY, (1997 Nov) 39 (11): 775-6.

Journal code: E83. ISSN: 0012-1622.

CY ENGLAND: United Kingdom

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199802

AB We report myositis ossificans occurring in a 13-year-old boy with severe and rapidly progressive Guillain-Barre syndrome. This complication should be considered when severe musculoskeletal pain is experienced by such patients. Disodium etidronate may be of benefit in this condition.

CT Check Tags: Case Report; Human; Male

Adolescence

Cerebrospinal Fluid Proteins: AN, analysis

Etidronate Disodium: TU, therapeutic use

Immunoglobulins, Intravenous: TU, therapeutic use

Myositis Ossificans: DI, diagnosis

Myositis Ossificans: DT, drug therapy

*Myositis Ossificans: ET, etiology

Pain: ET, etiology

Polyradiculoneuropathy: CF, cerebrospinal fluid

*Polyradiculoneuropathy: CO, complications

Polyradiculoneuropathy: TH, therapy

RN 7414-83-7 (Etidronate Disodium)

CN 0 (Cerebrospinal Fluid Proteins); 0 (Immunoglobulins, Intravenous)

L158 ANSWER 8 OF 30 MEDLINE

AN 97402354 MEDLINE

DN 97402354

TI Matrix metalloproteinase 13 (collagenase 3) in human rheumatoid synovium.

AU Lindy O; Konttinen Y T; Sorsa T; Ding Y; Santavirta S; Ceponis A;

Lopez-Otin C

CS University of Helsinki, Finland.

SO ARTHRITIS AND RHEUMATISM, (1997 Aug) 40 (8) 1391-9.

Journal code: 90M. ISSN: 0004-3591.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Abridged Index Medicus Journals; Priority Journals

EM 199711

EW 19971102

AB OBJECTIVE: To show the eventual presence and extent of production of matrix metalloproteinase 13 (MMP-13, or collagenase 3) in rheumatoid synovial tissue samples and extracts, and to assess the inhibition

characteristics of recombinant MMP-13. METHODS: Immunohistochemical avidin-biotin-peroxidase complex staining/morphometry was used to analyze MMP-13-positive cells in situ. Neutral salt extraction of synovial tissue, electrophoresis of the extract in different buffer systems, and Western blotting were also used. The inhibitory properties of doxycycline, clodronate, pamidronate, and D-penicillamine for recombinant enzyme were determined with a soluble type II collagen assay. RESULTS: MMP-13 was detected in fibroblast- and macrophage-like mononuclear cells in the synovial lining and stroma and in vascular endothelial cells. The overall expression of MMP-13 in these cells in the synovial stroma was high in rheumatoid arthritis (86 +/- 12%) compared with osteoarthritis (17 +/- 5%) patient samples (P = 0.0027). In a high-pH native electrophoresis gel, immunoreactivity to anti-MMP-1 and anti-MMP-13 were clearly separated, with anti-MMP-13-immunoreactive material migrating faster than anti-MMP-1-immunoreactive material. Finally, in contrast to MMP-1 and MMP-8, MMP-13 was found to be relatively resistant to the inhibitory effects of doxycycline and clodronate in vitro. CONCLUSION: Due to its localization in synovial tissue, its substrate profile, increased expression, and relative resistance to known MMP inhibitors, MMP-13 is suggested to play a major role in the pathogenesis of tissue destruction in rheumatoid arthritis.

CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't

Adult

Aged

Aged, 80 and over

*Arthritis, Rheumatoid: EN, enzymology

Arthritis, Rheumatoid: GE, genetics

Cartilage, Articular: CH, chemistry

Cartilage, Articular: EN, enzymology

Clodronic Acid: PD, pharmacology

Collagenases: AI, antagonists & inhibitors

*Collagenases: GE, genetics

Diphosphonates: PD, pharmacology

Immunoblotting

Immunohistochemistry

Middle Age

Osteoarthritis: EN, enzymology

Osteoarthritis: GE, genetics

Penicillamine: PD, pharmacology

Recombinant Proteins: GE, genetics

RNA, Messenger: ME, metabolism

Synovial Membrane: CH, chemistry

*Synovial Membrane: EN, enzymology

RN 10596-23-3 (Clodronic Acid); 40391-99-9 (amidronate);

52-67-5 (Penicillamine)

CN EC 3.4.24.- (collagenase 3); EC 3.4.24.- (Collagenases); 0

(Diphosphonates); 0 (Recombinant Proteins); 0 (RNA, Messenger)

L158 ANSWER 9 OF 30 MEDLINE

AN 97273642 MEDLINE

DN 97273642

TI Periarticular ectopic calcinosis probably due to 1 alpha-OH-vitamin D3 therapy, and successful treatment with bisphosphonate compound in a patient with systemic lupus erythematosus.

AU Miyata M; Kurokawa M; Watanabe S; Ishikawa H; Sekine H; Ito O; Nishimaki T; Kasukawa R

CS Department of Internal Medicine II, Fukushima Medical College, Japan.

SO FUKUSHIMA JOURNAL OF MEDICAL SCIENCE, (1996 Dec) 42 (1-2) 39-46.

Ref: 28

Journal code: F91. ISSN: 0016-2590.

CY Japan

DT Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)

(REVIEW OF REPORTED CASES)

LA English

EM 199707

EW 19970703
 AB We describe the case of a 25-year-old woman who developed soft tissue ectopic nephritis. Ectopic calcinosis rarely occurs in systemic lupus erythematosus (SLE) patients. This is the first detailed case report of metastatic ectopic calcinosis, one of two categories of ectopic calcinosis, probably due to 1 alpha-OH-vitamin D3 therapy. We administered disodium 3-amino-1-hydroxypropylidene-1, 1-bisphosphonate pentahydrate, a second-generation bisphosphonate, to decrease the patient's serum calcium level, and subsequently observed a dramatic decrease in severity of the ectopic calcinosis along with decreases in both the serum calcium level and the (serum calcium level)x(serum phosphate level) index. We suggest that 1 alpha-OH vitamin D3 should be used in cases of lupus nephritis with great caution.

CT Check Tags: Case Report; Female; Human
 Adult
 *Calcinosis: CI, chemically induced
 Calcinosis: DT, drug therapy
 *Diphosphonates: TU, therapeutic use
 *Finger Joint
 *Hydroxycholecalciferols: AE, adverse effects
 *Lupus Erythematosus, Systemic: CO, complications

RN 40391-99-9 (amidronate); 41294-56-8 (1-hydroxycholecalciferol)
 CN 0 (Diphosphonates); 0 (Hydroxycholecalciferols)

L158 ANSWER 10 OF 30 MEDLINE
 AN 96316377 MEDLINE
 DN 96316377
 TI [Generalized osteoporosis in chronic polyarthritis--pathomechanisms and treatment approaches].
 Generalisierte Osteoporose bei chronischer Polyarthritis--Pathomechanismen und Behandlungsansätze.

AU Ringe J D
 CS Medizinische Klinik IV, Klinikum Leverkusen, Akademisches Lehrkrankenhaus, Universität zu Köln.
 SO ZEITSCHRIFT FÜR RHEUMATOLOGIE, (1996 May-Jun) 55 (3) 149-57.
 Ref: 49
 Journal code: YOV. ISSN: 0340-1855.

CY GERMANY: Germany, Federal Republic of
 DT Journal; Article; (JOURNAL ARTICLE)
 General Review; (REVIEW)
 (REVIEW, TUTORIAL)

LA German
 FS Priority Journals
 EM 199612

AB Juxtaarticular osteoporosis is a typical x-ray symptom of rheumatoid arthritis and is an early radiological criterion of the disease before destructive changes of joints can be seen. A systemic osteoporosis, independent from corticoid treatment, will develop significantly later. Nevertheless both conditions have some pathogenetic mechanisms in common. The risk of generalized osteoporosis in rheumatoid arthritis correlates with the degree of inflammatory activity. Different cytokines originating from the affected joints can be measured in plasma at increased levels and augment osteoclastic activity in bone tissue. During the early phase of disease the best prevention of osteoporosis is therefore adequate suppression of inflammation. Taking into account these mechanisms, corticoid treatment may be osteoprotective. Clinical manifestation of systemic osteoporosis in rheumatic patients depends on bone mass at onset of disease, on the activity of inflammation, and on additional negative effects on bone mass due to corticoids and immobility.

CT Check Tags: Human
 Adrenal Cortex Hormones: AD, administration & dosage
 Adrenal Cortex Hormones: AE, adverse effects
 *Arthritis, Rheumatoid: CO, complications
 Arthritis, Rheumatoid: DI, diagnosis
 Arthritis, Rheumatoid: DT, drug therapy
 Bone Density: DE, drug effects

Bone Density: PH, physiology
 Calcitonin: AD, administration & dosage
 Calcium, Dietary: AD, administration & dosage
 Combined Modality Therapy
 Cytokines: BL, blood
Diphosphonates: AD, administration & dosage
 English Abstract
 Osteoclasts: DE, drug effects
 Osteoclasts: PH, physiology
 Osteoporosis: DI, diagnosis
 Osteoporosis: DT, drug therapy
 *Osteoporosis: ET, etiology
 Risk Factors
 Vitamin D: AD, administration & dosage

RN 1406-16-2 (Vitamin D); 9007-12-9 (Calcitonin)
 CN 0 (Adrenal Cortex Hormones); 0 (Calcium, Dietary); 0 (Cytokines); 0
(Diphosphonates)

L158 ANSWER 11 OF 30 MEDLINE

AN 96193600 MEDLINE

DN 96193600

TI Increased bone mass with pamidronate treatment in rheumatoid arthritis.
 Results of a three-year randomized, double-blind trial.

AU Eggelmeijer F; Papapoulos S E; van Paassen H C; Dijkmans B A; Valkema R;
 Westedt M L; Landman J O; Pauwels E K; Breedveld F C

CS University Hospital, Leiden, The Netherlands.

SO ARTHRITIS AND RHEUMATISM, (1996 Mar) 39 (3) 396-402.

Journal code: 90M. ISSN: 0004-3591.

CY United States

DT (CLINICAL TRIAL)

Journal; Article; (JOURNAL ARTICLE)

(RANDOMIZED CONTROLLED TRIAL)

LA English

FS Abridged Index Medicus Journals; Priority Journals

EM 199607

AB OBJECTIVES: Osteoporosis is a frequent complication of rheumatoid arthritis (RA). We therefore investigated the effect of oral pamidronate therapy as a specific bone-sparing agent in RA. METHODS: The study design was a 3-year randomized, double-blind trial of 300 mg oral pamidronate/day compared with placebo in 105 RA patients. Bone mineral density (BMD) measured at 12-month intervals was the primary efficacy parameter. RESULTS: In 3 years, lumbar spine and forearm BMD increased significantly in the pamidronate-treated group (by 8.4 +/- 6.9% [mean +/- SEMI] [P < 0.00011 and 5.2 +/- 6.5% [P < 0.005], respectively), compared with nonsignificant changes in the placebo-treated patients (increase of 0.6 +/- 5.2% and decrease of 1.2 +/- 5.8%, respectively). Femoral neck BMD increased in the pamidronate-treated group (by 2.6 +/- 8.6%) and decreased significantly in the placebo-treated group (by 4.0 +/- 1.3% [P < 0.005]). The changes in BMD with time at all 3 measurement sites were significantly different between the treatment groups (P < 0.0001). Changes in radiographic signs of joint damage and in disease activity were similar in the 2 groups. CONCLUSION: The present study provides the first evidence that long-term treatment with an orally administered bisphosphonate overcomes bone loss and increases bone mass when compared with placebo. This finding may have significance with regard to the treatment of patients with RA.

CT Check Tags: Female; Human; Male

Adult

Aged

Anti-Inflammatory Agents, Non-Steroidal: AD, administration & dosage

*Arthritis, Rheumatoid: DT, drug therapy

Arthritis, Rheumatoid: PA, pathology

Bone and Bones: DE, drug effects

Bone and Bones: ME, metabolism

*Bone and Bones: PA, pathology

Bone Density: DE, drug effects

***Diphosphonates: AD, administration & dosage**

Diphosphonates: TO, toxicity

Double-Blind Method

Injections, Intravenous

Middle Age

Placebos

Walking

RN **40391-99-9 (amidronate)**

CN 0 (Anti-Inflammatory Agents, Non-Steroidal); 0 (Diphosphonates);

0 (Placebos)

L158 ANSWER 12 OF 30 MEDLINE

AN 96111183 MEDLINE

DN 96111183

TI Treatment of osteoporosis of rheumatoid arthritis [letter].

AU Cantatore F P; Carrozzo M

SO CLINICAL RHEUMATOLOGY, (1995 Sep) 14 (5) 594-5.

Journal code: DI6. ISSN: 0770-3198.

CY Belgium

DT Letter

LA English

FS Priority Journals

EM 199604

CT Check Tags: Human

***Arthritis, Rheumatoid: CO, complications**

Diphosphonates: TU, therapeutic use

***Osteoporosis: DT, drug therapy**

***Osteoporosis: ET, etiology**

Osteoporosis: PP, physiopathology

CN **0 (Diphosphonates)**

L158 ANSWER 13 OF 30 MEDLINE

AN 95404532 MEDLINE

DN 95404532

TI Low dose corticosteroid associated osteoporosis in rheumatoid arthritis and its prophylaxis and treatment: bones of contention [editorial].

AU Dequeker J; Westhovens R

SO JOURNAL OF RHEUMATOLOGY, (1995 Jun) 22 (6) 1013-9. Ref: 66

Journal code: JWX. ISSN: 0315-162X.

CY Canada

DT Editorial

General Review; (REVIEW)

(REVIEW, TUTORIAL)

LA English

FS Priority Journals

EM 199512

CT Check Tags: Female; Human

***Adrenal Cortex Hormones: AE, adverse effects**

Adrenal Cortex Hormones: TU, therapeutic use

***Arthritis, Rheumatoid: DT, drug therapy**

Bone Density: DE, drug effects

Diphosphonates: TU, therapeutic use

Dose-Response Relationship, Drug

Estrogen Replacement Therapy

Fluorides: TU, therapeutic use

***Osteoporosis: CI, chemically induced**

***Osteoporosis: PC, prevention & control**

Osteoporosis: TH, therapy

Vitamin D: ME, metabolism

RN 1406-16-2 (Vitamin D)

CN 0 (Adrenal Cortex Hormones); 0 (Diphosphonates); 0 (Fluorides)

L158 ANSWER 14 OF 30 MEDLINE

AN 95362762 MEDLINE

DN 95362762

TI Glucocorticoid-induced osteoporosis.

AU Hahn B H; Mazzaferri E L
 CS University of California School of Medicine, Los Angeles, USA..
 SO HOSPITAL PRACTICE (OFFICE EDITION), (1995 Aug 15) 30 (8) 45-9,
 52-3; discussion 53-6.
 Journal code: HPO. ISSN: 8750-2836.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Abridged Index Medicus Journals; Priority Journals
 EM 199511
 AB High-dose treatment of more than three months' duration reduces bone mass,
 regardless of the patient's age, sex, or race. Because bone loss is most
 severe during the first six to 12 months of treatment, prophylaxis to
 preserve bone--with calcium, vitamin D, a bisphosphonate, and
 exercise--should begin as soon as the clinical situation permits rather
 than after the disease has been brought under control.

CT Check Tags: Case Report; Female; Human
 Adolescence
 Aged
 Calcium: TU, therapeutic use
 Combined Modality Therapy
Diphosphonates: TU, therapeutic use
 Drug Therapy, Combination
 Exercise Therapy
 Glucocorticoids, Synthetic: AD, administration & dosage
 *Glucocorticoids, Synthetic: AE, adverse effects
 Iatrogenic Disease: PC, prevention & control
Lupus Erythematosus, Systemic: CO, complications
Lupus Erythematosus, Systemic: DT, drug therapy
 *Osteoporosis: CI, chemically induced
 Osteoporosis: PC, prevention & control
 Polymyalgia Rheumatica: CO, complications
 Polymyalgia Rheumatica: DT, drug therapy
 Prednisone: AD, administration & dosage
 Prednisone: AE, adverse effects
 Time Factors
 Vitamin D: TU, therapeutic use

RN 1406-16-2 (Vitamin D); 53-03-2 (Prednisone); 7440-70-2 (Calcium)
 CN 0 (**Diphosphonates**); 0 (Glucocorticoids, Synthetic)

L158 ANSWER 15 OF 30 MEDLINE
 AN 95262295 MEDLINE
 DN 95262295
 TI Macrophages in T cell line-mediated, demyelinating, and chronic relapsing
 experimental autoimmune encephalomyelitis in Lewis rats.
 AU Huitinga I; Ruuls S R; Jung S; Van Rooijen N; Hartung H P; Dijkstra C D
 CS Department of Cell Biology and Immunology, Faculty of Medicine, Vrije
 Universiteit, Amsterdam, The Netherlands.
 SO CLINICAL AND EXPERIMENTAL IMMUNOLOGY, (1995 May) 100 (2) 344-51.
 Journal code: DD7. ISSN: 0009-9104.
 CY ENGLAND: United Kingdom
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals; Cancer Journals
 EM 199508
 AB About 50% of the mononuclear cells in the perivascular lesions in the
 central nervous system (CNS) of rats suffering from experimental allergic
 encephalomyelitis (EAE) are blood-borne macrophages. In this study we
 investigated the role of these macrophages in different variants of EAE,
 using a liposome-mediated macrophage depletion technique. Intravenously
 injected liposomes containing dichloromethylene diphosphonate (Cl2MDP) are
 ingested by macrophages and cause temporary and selective elimination of
 these cells. Macrophage depletion during EAE induced by a T cell line
 specific for myelin basic protein (MBP; T cell-EAE) suppresses development
 of neurological signs of EAE. T cell-EAE with pronounced demyelination as
 induced by an additionally injected MoAb directed against myelin

oligodendrocyte glycoprotein (MOG) was also significantly ameliorated after macrophage depletion. During chronic relapsing EAE (CR-EAE) the occurrence of relapses was prevented or suppressed, provided that the liposomes were injected before the initiation of a putative relapse. A chronic progressive course of CR-EAE was not modified by Cl2MDP containing liposome treatment. Histologic examination of the CNS of liposome-treated animals confirmed decreased infiltration of macrophages into the parenchyma in the rats with T cell and AD-EAE, whereas T cells were still present.

CT Check Tags: Animal; Male; Support, Non-U.S. Gov't

Clodronic Acid: PD, pharmacology

Cyclosporine: PD, pharmacology

Demyelinating Diseases: IM, immunology

*Encephalomyelitis, Experimental Autoimmune: IM, immunology

Encephalomyelitis, Experimental Autoimmune: PA, pathology

*Macrophages: IM, immunology

Rats

Rats, Inbred Lew

T-Lymphocytes: IM, immunology

RN 10596-23-3 (Clodronic Acid); 59865-13-3 (Cyclosporine)

L158 ANSWER 16 OF 30 MEDLINE

AN 95173891 MEDLINE

DN 95173891

TI Clinical and biochemical response to single infusion of pamidronate in patients with active rheumatoid arthritis: a double blind placebo controlled study.

AU Eggelmeijer F; Papapoulos S E; van Paassen H C; Dijkmans B A; Breedveld F C

CS Department of Rheumatology, Leiden, The Netherlands..

SO JOURNAL OF RHEUMATOLOGY, (1994 Nov) 21 (11) 2016-20.

Journal code: JWX. ISSN: 0315-162X.

CY Canada

DT (CLINICAL TRIAL)

Journal; Article; (JOURNAL ARTICLE)

(RANDOMIZED CONTROLLED TRIAL)

LA English

FS Priority Journals

EM 199506

AB OBJECTIVE. To assess the effects of 3-amino-1-hydroxypropylidene-1,1-bisphosphonate (pamidronate) in rheumatoid arthritis (RA). METHODS. Thirty patients with active RA were randomly allocated to receive a single intravenous infusion of placebo, 20 mg pamidronate, or 40 mg pamidronate. RESULTS. Pamidronate treatment resulted in a rapid and sustained reduction in urinary calcium and hydroxyproline excretions. A sustained reduction in serum corrected calcium was only noted in the group treated with 40 mg pamidronate. In both groups treated with pamidronate a temporary increase in serum parathyroid hormone was noted. Compared to the placebo group clinical variables of disease activity improved significantly in both groups treated with aminohydroxypropylidene bisphosphonate. The erythrocyte sedimentation rate and serum C-reactive protein levels improved significantly in patients treated with 40 mg pamidronate. No serious side effects were documented. CONCLUSION. A single infusion of pamidronate in patients with RA is safe, suppresses bone resorption, and reduces disease activity. It is suggested that the effect on disease activity is dose dependent.

CT Check Tags: Comparative Study; Female; Human; Male
Adult

Arthritis, Rheumatoid: BL, blood

*Arthritis, Rheumatoid: DT, drug therapy

Arthritis, Rheumatoid: ME, metabolism

Arthritis, Rheumatoid: UR, urine

Bone and Bones: DE, drug effects

*Bone and Bones: ME, metabolism

Bone Resorption: DT, drug therapy

Calcium: BL, blood

Calcium: UR, urine
 Diphosphonates: AE, adverse effects
 *Diphosphonates: TU, therapeutic use
 Double-Blind Method
 Hydroxyproline: UR, urine
 Infusions, Intravenous
 Middle Age
 Radioimmunoassay

RN 40391-99-9 (amidronate); 51-35-4 (Hydroxyproline); 7440-70-2
 (Calcium)
 CN 0 (Diphosphonates)

L158 ANSWER 17 OF 30 MEDLINE

AN 95138952 MEDLINE

DN 95138952

TI Intermittent cyclic therapy with etidronate in the prevention of
 corticosteroid induced bone loss.

AU Adachi J; Cranney A; Goldsmith C H; Bensen W G; Bianchi F; Cividino A;
 Craig G L; Kaminska E; Sebaldt R J; Papaioannou A; et al

CS St. Joseph's Hospital, McMaster University, Hamilton, ON, Canada..

SO JOURNAL OF RHEUMATOLOGY, (1994 Oct) 21 (10) 1922-6.

Journal code: JWX. ISSN: 0315-162X.

CY Canada

DT (CLINICAL TRIAL)

Journal; Article; (JOURNAL ARTICLE)

(RANDOMIZED CONTROLLED TRIAL)

LA English

FS Priority Journals

EM 199505

AB OBJECTIVE. To assess the potential efficacy of intermittent cyclic therapy
 (ICT) with etidronate in the treatment of patients with corticosteroid
 induced osteoporosis. METHODS. Cohort study in a tertiary care university
 affiliated hospital in corticosteroid treated patients, with polymyalgia
 rheumatica, asthma, systemic lupus erythematosus, rheumatoid arthritis, or
 temporal arteritis, examining the effects of ICT etidronate. Patients were
 included if they were taking corticosteroids for a minimum of one year.
 Comparison patients were those who had been taking corticosteroids for a
 minimum of one year and who had not been treated with etidronate or other
 medication which might alter bone metabolism. A total of 68 patients were
 included from 253 considered. The mean (SD) dose of prednisone in the ICT
 etidronate treated patients was 9.3 (6.2) mg and in the comparison
 patients 9.4 (5.9) mg. The duration of prednisone therapy was 7.8 (5.8)
 years and 3.4 (4.2) years, respectively ($p_2 < 0.001$). An analysis of
 covariance demonstrated that this difference did not alter our primary
 outcome measure. The primary outcome measure was the difference in the
 percentage change from baseline to one year of followup in bone mineral
 density (BMD) of the lumbar spine between treatment and comparison groups.
 RESULTS. ICT etidronate resulted in a statistically significant and
 clinically important increase in BMD. The BMD of the lumbar spine
 increased by 3.82% (0.65%), [95% confidence interval (CI), 2.51 to 5.14%]
 in the 35 ICT etidronate treated patients and decreased by 1.78% (0.76%),
 [95% CI, -3.34 to -0.23%] in the 33 comparison patients after 12 months
 ($p_2 < 0.0001$). CONCLUSIONS. ICT etidronate prevented loss of vertebral
 bone density in patients with corticosteroid induced osteoporosis.
 Controlled, double blind, prospective trials with longer followup are
 needed to confirm these results and to demonstrate that increases in bone
 mass translate into decreased fracture rates.

CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't

*Adrenal Cortex Hormones: AE, adverse effects

Adrenal Cortex Hormones: TU, therapeutic use

Adult

Aged

Arthritis, Rheumatoid: DT, drug therapy

Bone Density

Cohort Studies

Dose-Response Relationship, Drug

Double-Blind Method
 Etidronate Disodium: AD, administration & dosage
 *Etidronate Disodium: TU, therapeutic use
 Femur Neck: PH, physiology
 Follow-Up Studies
 Lumbar Vertebrae: PH, physiology
Lupus Erythematosus, Systemic: DT, drug therapy
 Middle Age
 *Osteoarthritis: CI, chemically induced
 *Osteoarthritis: PC, prevention & control
 Pilot Projects

RN **7414-83-7 (Etidronate Disodium)**
 CN 0 (Adrenal Cortex Hormones)

L158 ANSWER 18 OF 30 MEDLINE

AN 94377906 MEDLINE

DN 94377906

TI Double blind radiological assessment of continuous oral pamidronic acid in patients with rheumatoid arthritis.

AU Maccagno A; Di Giorgio E; Roldan E J; Caballero L E; Perez Lloret A

CS Department of Rheumatology, French Hospital, Buenos Aires, Argentina.

SO SCANDINAVIAN JOURNAL OF RHEUMATOLOGY, (1994) 23 (4) 211-4.

Journal code: UD1. ISSN: 0300-9742.

CY Norway

DT (CLINICAL TRIAL)

Journal; Article; (JOURNAL ARTICLE)

(RANDOMIZED CONTROLLED TRIAL)

LA English

FS Priority Journals

EM 199412

AB Continuous oral pamidronate (APD), 1000 mg/day, was administered to 14 patients with rheumatoid arthritis. A control group of 13 patients with similar conditions received placebo under a double blind randomized study design. Periarticular erosion scores were significantly higher in the control group after 12 months treatment. This was attributed to a deterioration in this group rather than to an improvement in the APD treated one. By contrast, intraarticular narrowing score was not influenced by APD. Tolerance to oral APD was acceptable in all patients.

CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't
 Administration, Oral
 Adult

Arthritis, Rheumatoid: DT, drug therapy

***Arthritis, Rheumatoid: RA, radiography**

Cartilage, Articular: RA, radiography

***Diphosphonates: AD, administration & dosage**

Double-Blind Method

Drug Administration Schedule

Foot: RA, radiography

Hand: RA, radiography

Middle Age

Severity of Illness Index

RN **40391-99-9 (amidronate)**

CN 0 (Diphosphonates)

L158 ANSWER 19 OF 30 MEDLINE

AN 94207702 MEDLINE

DN 94207702

TI Intermittent cyclical etidronate in the prevention of corticosteroid-induced bone loss.

AU Mulder H; Struys A

CS Gezondheidscentrum Zuidplein, Rotterdam, The Netherlands.

SO BRITISH JOURNAL OF RHEUMATOLOGY, (1994 Apr) 33 (4) 348-50.

Journal code: B1T. ISSN: 0263-7103.

CY ENGLAND: United Kingdom

DT (CLINICAL TRIAL)

(CONTROLLED CLINICAL TRIAL)

Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Abridged Index Medicus Journals; Priority Journals
 EM 199407
 AB We conducted a prospective study of etidronate's effects on corticosteroid-induced bone loss in postmenopausal women with temporal arteritis for whom high-dose prednisone therapy was indicated. Group A (n = 10) received etidronate (400 mg/day for 2 weeks, then 11 weeks off etidronate; four cycles total) and prednisone: Group B (n = 10) received only prednisone. Vertebral bone mineral density (BMD) was measured blinded by dual X-ray absorptiometry. At 3, 6 and 12 months, vertebral BMD was significantly ($P < 0.01$) increased in Group A and decreased in Group B, based on mean actual and percent changes in BMD and mean changes in BMD Z-score from baseline. Between-group comparisons were also significant ($P < 0.002$) at each time point. No adverse events related to etidronate treatment were reported. Our results suggest that corticosteroid-induced bone loss may be prevented by instituting intermittent cyclical etidronate therapy when high-dose prednisone therapy is begun. Further research into bisphosphonate use in corticosteroid-induced bone loss (with larger patient populations, longer follow-up and fracture assessment) is warranted.

CT Check Tags: Female; Human
 *Adrenal Cortex Hormones: AE, adverse effects
 Aged
 Aged, 80 and over
 Bone Density: DE, drug effects
 Drug Administration Schedule
 *Etidronate Disodium: AE, adverse effects
 Etidronate Disodium: TU, therapeutic use
 Middle Age
 *Osteoporosis, Postmenopausal: CI, chemically induced
 Osteoporosis, Postmenopausal: ME, metabolism
 Prednisone: AD, administration & dosage
 Prednisone: AE, adverse effects
 Prednisone: TU, therapeutic use
 Temporal Arteritis: DT, drug therapy

RN 53-03-2 (Prednisone); 7414-83-7 (Etidronate Disodium)
 CN 0 (Adrenal Cortex Hormones)

L158 ANSWER 20 OF 30 MEDLINE
 AN 94103837 MEDLINE
 DN 94103837
 TI Selective elimination of macrophages by dichlormethylene diphosphonate-containing liposomes suppresses experimental autoimmune neuritis.
 AU Jung S; Huitinga I; Schmidt B; Zielasek J; Dijkstra C D; Toyka K V; Hartung H P
 CS Department of Neurology, Julius-Maximilians-Universitat, Wurzburg, Germany..
 SO JOURNAL OF THE NEUROLOGICAL SCIENCES, (1993 Nov) 119 (2) 195-202.
 Journal code: JBJ. ISSN: 0022-510X.
 CY Netherlands
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 199404
 AB The injection of liposome-encapsulated dichlormethylene diphosphonate (Cl2MDP) constitutes an effective method to selectively eliminate phagocytic cells from spleen, liver and the circulation. We evaluated the effect of Cl2MDP-liposomes on the course of actively induced and adoptively transferred experimental autoimmune neuritis (EAN), both animal models of the human Guillain-Barre syndrome. Injection of Cl2MDP-liposomes 11 and 13 days postimmunization (p.i.) of Lewis rats with bovine peripheral nerve myelin efficiently prevented clinical signs of EAN up to day 15 p.i., when all control animals were affected. Thereafter, EAN

gradually also developed in Cl2MDP-liposome-treated rats, but until day 19 disease was significantly milder than in control rats injected with buffer-filled liposomes. Adoptive transfer EAN (AT-EAN) induced by injection of activated P2-specific T cells could be suppressed even more markedly by application of Cl2MDP-liposomes 1, 3, and 6 days after cell transfer. Efficient suppression of AT-EAN by Cl2MDP-liposomes rules out the possibility that EAN is prevented due to interference with the induction phase of this experimental disease and confirms that macrophages are important effector cells during EAN. Selective suppression of phagocytic cell function by drug-containing liposomes may hold promise as a novel treatment of demyelinating autoimmune diseases of the nervous system.

CT Check Tags: Animal; Female; Support, Non-U.S. Gov't
Behavior, Animal: PH, physiology

*Clodronic Acid: PD, pharmacology

Electrophysiology

Liposomes

*Macrophages: DE, drug effects

Myelin Sheath: IM, immunology

*Neuritis, Experimental Allergic: IM, immunology

Neuritis, Experimental Allergic: PA, pathology

Neuritis, Experimental Allergic: PX, psychology

Rats

Rats, Inbred Lew

Sciatic Nerve: PA, pathology

Spinal Nerve Roots: PA, pathology

RN 10596-23-3 (Clodronic Acid)

CN 0 (Liposomes)

L158 ANSWER 21 OF 30 MEDLINE

AN 91284442 MEDLINE

DN 91284442

TI Treatment and prevention of osteoporosis in juvenile chronic arthritis with disodium clodronate.

AU Lepore L; Pennesi M; Barbi E; Pozzi R

CS Pediatric Department, University of Trieste, Istituto per l'Infanzia Burlo Garofolo, Italy.

SO CLINICAL AND EXPERIMENTAL RHEUMATOLOGY, (1991 Jan-Feb) 9 Suppl 6 33-5.

Journal code: DFA. ISSN: 0392-856X.

CY Italy

DT (CLINICAL TRIAL)

(CONTROLLED CLINICAL TRIAL)

Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199110

AB Osteoporosis is one of the most difficult problems in the management of Chronic Juvenile Arthritis (JCA). The available data suggest that bone loss results from multifactorial processes which lead to bone degradation through the activation of osteoclasts. Biphosphonates are synthetic factors that, once localized on the surface of hydroxyapatite crystals, do not allow either the production or destruction of the crystals. This activity seems to be due to cytotoxicity against osteoclasts and to inhibition of prostaglandin E2 synthesis. There is some evidence that these drugs are effective in the treatment of osteoporosis in several diseases. In an attempt to reduce or prevent osteoporosis in children affected by JCA we started a trial with disodium clodronate, a type of biphosphonate. Thirteen patients were enrolled in the study: 7 received disodium clodronate and 6 acted as control subjects. Before starting the therapy and after one year we performed a CT scan to evaluate the mineral bone density in all patients. The mean bone density increased from a bone mineral content of 129 mg/cc before treatment to 134 mg/cc after treatment (8% increase); control patients passed from 123 mg/cc to 115 mg/cc (7% decrease) in the same period. Only one child stopped treatment because of gastrointestinal side effects. The small number of patients enrolled in

the trial does not allow any definite conclusions to be drawn, but the data are interesting and worthy of further study.

CT Check Tags: Human
Arthritis, Juvenile Rheumatoid: CO, complications
***Arthritis, Juvenile Rheumatoid: DT, drug therapy**
Arthritis, Juvenile Rheumatoid: ME, metabolism
 Bone Density: DE, drug effects
 Calcium: BL, blood
 Calcium: UR, urine
 Child
 Child, Preschool
Diphosphonates: AE, adverse effects
***Diphosphonates: TU, therapeutic use**
 Osteoporosis: ET, etiology
***Osteoporosis: PC, prevention & control**
 RN 7440-70-2 (Calcium)
 CN 0 (Diphosphonates)

L158 ANSWER 22 OF 30 MEDLINE
 AN 91279593 MEDLINE
 DN 91279593
 TI Endocrinology.
 AU Baxter M A; Sheppard M C
 CS Department of Medicine, University of Birmingham, Queen Elizabeth Hospital, Edgbaston, UK..
 SO POSTGRADUATE MEDICAL JOURNAL, (1991 Jan) 67 (783) 23-32. Ref: 47
 Journal code: PFX. ISSN: 0032-5473.
 CY ENGLAND: United Kingdom
 DT Journal; Article; (JOURNAL ARTICLE)
 General Review; (REVIEW)
 (REVIEW, TUTORIAL)
 LA English
 FS Priority Journals
 EM 199110
 CT Check Tags: Human
 Adult
Diphosphonates: TU, therapeutic use
***Endocrine Diseases: TH, therapy**
Graves' Disease: DT, drug therapy
 Hypercalcemia: ET, etiology
 Neoplasms: CO, complications
 Osteoporosis: CI, chemically induced
 Ovulation Induction
 Proteins: PH, physiology
 Somatotropin: PH, physiology
 Somatotropin: TU, therapeutic use
 Thyroid Hormones: PH, physiology
 Thyroxine: AE, adverse effects
 Turner's Syndrome: DT, drug therapy
 RN 7488-70-2 (Thyroxine); 9002-72-6 (Somatotropin)
 CN 0 (parathyroid hormone-related protein); 0 (Diphosphonates); 0 (Thyroid Hormones)

L158 ANSWER 23 OF 30 MEDLINE
 AN 91191305 MEDLINE
 DN 91191305
 TI Osteoporosis in rheumatoid arthritis--the clinical viewpoint [editorial].
 AU Woolf A D
 SO BRITISH JOURNAL OF RHEUMATOLOGY, (1991 Apr) 30 (2) 82-4.
 Journal code: B1T. ISSN: 0263-7103.
 CY ENGLAND: United Kingdom
 DT Editorial
 LA English
 FS Abridged Index Medicus Journals; Priority Journals
 EM 199107

CT Check Tags: Human
 Anti-Inflammatory Agents: TU, therapeutic use
 *Arthritis, Rheumatoid: CO, complications
 Arthritis, Rheumatoid: PA, pathology
 Arthritis, Rheumatoid: PP, physiopathology
 Biological Markers
 Bone and Bones: PA, pathology
 Bone Diseases, Metabolic: CO, complications
 Diphosphonates: TU, therapeutic use
 Estrogens: TU, therapeutic use
 Osteogenesis
 *Osteoporosis: CO, complications
 Osteoporosis: DT, drug therapy

CN 0 (Biological Markers); 0 (Diphosphonates); 0 (Estrogens)

L158 ANSWER 24 OF 30 MEDLINE
 AN 91011242 MEDLINE
 DN 91011242
 TI Suppression of experimental allergic encephalomyelitis in Lewis rats after elimination of macrophages.
 AU Huitinga I; van Rooijen N; de Groot C J; Uitdehaag B M; Dijkstra C D
 CS Department of Cell Biology, Medical Faculty, Vrije Universiteit, Amsterdam, The Netherlands.
 SO JOURNAL OF EXPERIMENTAL MEDICINE, (1990 Oct 1) 172 (4) 1025-33.
 Journal code: I2V. ISSN: 0022-1007.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals; Cancer Journals
 EM 199101
 AB Almost 50% of the cells infiltrating the central nervous system (CNS) of animals with experimental allergic encephalomyelitis (EAE) are macrophages (M psi). To investigate the role of the M psi in the pathogenesis of EAE, we eliminated M psi by means of mannosylated liposomes containing dichloromethylene diphosphonate (Cl2MDP). Cl2MDP-containing liposomes injected intravenously eliminate M psi in spleen and liver. Incorporation of mannose into the lipid layers enables the liposomes to pass the blood-brain barrier (BBB). Injections of Cl2MDP-containing mannose liposomes intravenously shortly before the appearance of clinical signs, markedly suppressed the expression of clinical signs of EAE. This suppression was accompanied by a marked reduction of infiltrated M psi in the CNS. Cl2MDP-containing liposomes without mannose incorporated had no effect. Cl2MDP-containing mannosylated liposomes had no effect on plasma corticosterone levels compared with injections of saline; thus, the suppression of expression of EAE was not corticosterone mediated. These results show that the M psi within the CNS play an important role in the pathogenesis of EAE.

CT Check Tags: Animal; Male; Support, Non-U.S. Gov't
 Antigens, CD4: PH, physiology
 Brain: PA, pathology
 Clodronic Acid: AD, administration & dosage
 Clodronic Acid: PD, pharmacology
 Corticosterone: BL, blood
 *Encephalomyelitis, Experimental Autoimmune: ET, etiology
 Encephalomyelitis, Experimental Autoimmune: PA, pathology
 Encephalomyelitis, Experimental Autoimmune: PC, prevention & control
 Liposomes
 *Macrophages: PH, physiology
 Rats
 Rats, Inbred Lew
 T-Lymphocytes: PH, physiology

RN 10596-23-3 (Clodronic Acid); 50-22-6 (Corticosterone)
 CN 0 (Antigens, CD4); 0 (Liposomes)

L158 ANSWER 25 OF 30 MEDLINE

AN 89303431 MEDLINE
 DN 89303431
 TI Effects of aminobisphosphonate infusion on biochemical indices of bone metabolism in rheumatoid arthritis.
 AU Tan P L; Ames R; Yeoman S; Ibbertson H K; Caughey D E
 CS Department of Immunobiology, University of Auckland School of Medicine, New Zealand..
 SO BRITISH JOURNAL OF RHEUMATOLOGY, (1989 Aug) 28 (4) 325-8.
 Journal code: B1T. ISSN: 0263-7103.
 CY ENGLAND: United Kingdom
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Abridged Index Medicus Journals; Priority Journals
 EM 198910
 AB In a phase 1 study, seven patients with classical rheumatoid arthritis were treated with intravenous 3-amino-1-hydroxypropylidene-1-1-bisphosphonate (APD). Following this treatment, bone resorption as measured by fasting urine calcium/creatinine and hydroxyproline/creatinine ratios, was reduced. This was sustained for 6 months in only three patients. Elevations of these ratios often coincided with flares of active arthritis in the remaining four patients. Bone turnover as measured by serum osteocalcin levels was reduced in all patients but serum alkaline phosphatase levels remained unchanged. There was no consistent improvement in clinical indices of disease activity.
 CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't
 Adult
 Aged
 Arthritis, Rheumatoid: DT, drug therapy
 *Arthritis, Rheumatoid: UR, urine
 Bone and Bones
 Calcium: UR, urine
 Calcium-Binding Proteins: BL, blood
 Creatinine: UR, urine
 Diphosphonates: AD, administration & dosage
 *Diphosphonates: TU, therapeutic use
 Drug Evaluation
 Hydroxyproline: UR, urine
 Infusions, Intravenous
 Middle Age
 RN 104982-03-8 (Osteocalcin); 40391-99-9 (amidronate); 51-35-4 (Hydroxyproline); 60-27-5 (Creatinine); 7440-70-2 (Calcium)
 CN 0 (Calcium-Binding Proteins); 0 (Diphosphonates)

L158 ANSWER 26 OF 30 MEDLINE
 AN 89272261 MEDLINE
 DN 89272261
 TI Clinical, biochemical, and radiographic effects of aminohydroxypropylidene bisphosphonate treatment in rheumatoid arthritis.
 AU Ralston S H; Hacking L; Willocks L; Bruce F; Pitkeathly D A
 CS Medical Unit A, Southern General Hospital, Glasgow.
 SO ANNALS OF THE RHEUMATIC DISEASES, (1989 May) 48 (5) 396-9.
 Journal code: 62W. ISSN: 0003-4967.
 CY ENGLAND: United Kingdom
 DT (CLINICAL TRIAL)
 (CONTROLLED CLINICAL TRIAL)
 Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 198909
 AB A placebo controlled, double blind study of aminohydroxypropylidene bisphosphonate (APD), given by monthly intravenous infusion, was conducted in 40 patients with rheumatoid arthritis. Biochemical markers of increased bone resorption, such as fasting urinary calcium/creatinine ratio and hydroxyproline/creatinine ratio, were suppressed significantly in the APD group to approximately 50% and 60% of the pretreatment level respectively, and serum calcium fell transiently after the first APD infusion. There was

no significant effect on disease activity in either the APD or placebo groups as judged by clinical (grip strength, morning stiffness, visual analogue score) or laboratory (haemoglobin, platelet count, erythrocyte sedimentation rate, C reactive protein) criteria. An exception was the articular index which improved to a similar degree in both groups, falling from (mean (SEM) 13.8 (1.8) to 7.2 (2.2) in the APD group and from 13.7 (1.9) to 6.8 (1.5) in the placebo group. Radiological progression occurred to a similar degree in both groups as assessed by the Sharp index (mean (SEM) 86 (13.1) v 95 (12.9)-APD group; 103 (15.1) v 110 (15.8)-placebo group), but there was no significant change in the Larsen index in either group (mean (SEM) 53 (4.2) v 57 (3.8)-APD; 62 (5.8) v 63 (5.6)-placebo). The lack of effect on radiological progression in the APD group indicates that focal erosive disease may either have progressed as the result of a non-osteoclast related mechanism, or that the intensity of bone resorption was too great to be inhibited by the doses of APD used. (ABSTRACT TRUNCATED AT 250 WORDS)

CT Check Tags: Female; Human; Male

*Arthritis, Rheumatoid: DT, drug therapy

Arthritis, Rheumatoid: ME, metabolism

Arthritis, Rheumatoid: RA, radiography

Calcium: UR, urine

Clinical Trials

Creatinine: UR, urine

*Diphosphonates: TU, therapeutic use

Double-Blind Method

Hydroxyproline: UR, urine

Middle Age

Random Allocation

RN 40391-99-9 (amidronate); 51-35-4 (Hydroxyproline); 60-27-5 (Creatinine); 7440-70-2 (Calcium)

CN 0 (Diphosphonates)

L158 ANSWER 27 OF 30 MEDLINE

AN 88311750 MEDLINE

DN 88311750

TI A clinical and biochemical assessment of etidronate disodium in patients with active rheumatoid arthritis.

AU Bird H A; Hill J; Sittou N G; Dixon J S; Wright V

CS Clinical Pharmacology Unit, Royal Bath Hospital, Harrogate, United Kingdom..

SO CLINICAL RHEUMATOLOGY, (1988 Mar) 7 (1) 91-4.

Journal code: DI6. ISSN: 0770-3198.

CY Belgium

DT (CLINICAL TRIAL)

Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 198812

AB Diphosphonates reduce the rate of bone turnover. They have additional pharmacological properties improving adjuvant arthritis in rats and lowering ESR in this condition. We have evaluated etidronate disodium, a diphosphonate commonly prescribed in the United Kingdom for Paget's disease in patients with rheumatoid arthritis. Apart from an early improvement in articular index, perhaps reflecting anti-inflammatory activity, no significant change occurred in clinical variables or in laboratory indices of 'secondline' action at a dose of 5 mg/kg/day.

CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't

Adult

Aged

Arthritis, Rheumatoid: BL, blood

*Arthritis, Rheumatoid: DT, drug therapy

Arthritis, Rheumatoid: PP, physiopathology

Blood Sedimentation

Bone and Bones: PP, physiopathology

Clinical Trials

Etidronate Disodium: AE, adverse effects

*Etidronate Disodium: TU, therapeutic use
Gastrointestinal Diseases: CI, chemically induced
Middle Age
Pain: CI, chemically induced

RN 7414-83-7 (Etidronate Disodium)

L158 ANSWER 28 OF 30 MEDLINE

AN 87152757 MEDLINE

DN 87152757

TI Effect of (chloro-4-phenyl) thiomethylene bisphosphonic acid (SR 41319) on the autoimmune disease activity in MRL/l mice.

AU Barbier A; Planchenault C; Brelriere J C

SO AGENTS AND ACTIONS, (1986 Dec) 19 (5-6) 311-2.

Journal code: 2XZ. ISSN: 0065-4299.

CY Switzerland

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 198706

AB MRL - lpr/lpr (MRL/l) mice spontaneously develop an autoimmune pathology including arthritic lesions. SR 41319, a bisphosphonate, having previously shown to be active in in vitro and in vivo models of arthritis, the aim of this study was to search for its possible effect on the pathology of the MRL/l mice. Results showed that SR 41319 reduced the severity of the disease in its early stages and increased mean life span. Further investigation would be necessary to define the effect of the drug during later stages when major changes in immune status occurred.

CT Check Tags: Animal

*Autoimmune Diseases: IM, immunology

Autoimmune Diseases: PA, pathology

*Diphosphonates: PD, pharmacology

*Lupus Erythematosus, Systemic: IM, immunology

Lupus Erythematosus, Systemic: PA, pathology

Mice

Mice, Inbred Strains

*Phospholipases: AI, antagonists & inhibitors

*Phospholipases A: AI, antagonists & inhibitors

RN 96538-83-9 (SR 41319)

CN EC 3.1.- (Phospholipases); EC 3.1.1.- (Phospholipases A); 0
(Diphosphonates)

L158 ANSWER 29 OF 30 MEDLINE

AN 86268177 MEDLINE

DN 86268177

TI Immobilization hypercalcemia associated with Landry-Guillain-Barre syndrome. Successful therapy with combined calcitonin and etidronate.

AU Meythaler J M; Korkor A B; Nanda T; Kumar N A; Fallon M

SO ARCHIVES OF INTERNAL MEDICINE, (1986 Aug) 146 (8) 1567-71.

Journal code: 7FS. ISSN: 0003-9926.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals

EM 198610

AB Two patients with immobilization hypercalcemia associated with Landry-Guillain-Barre syndrome had marked hypercalciuria (890 and 1136 mg/d [22.2 and 28.3 mmol/d]) and radiologic evidence of generalized osteopenia. Parathyroid hormone levels were either low or normal by C-terminal radioimmunoassay. Subtotal parathyroidectomy was performed in the one patient, with no improvement in serum or urinary calcium levels. A bone biopsy specimen revealed decreased cellular activity in the first patient and increased bone resorption in the second patient. Treatment with intravenous saline, furosemide, oral phosphate supplementation, mithramycin, and calcitonin alone was ineffective in lowering serum or urinary calcium levels. However, when subcutaneous calcitonin combined with oral etidronate disodium was used, a reduction in the serum calcium

level was observed within two days of therapy. Within one week of the start of this combined therapy, the calcium level returned to normal and urinary calcium excretion was substantially reduced.

CT Check Tags: Case Report; Human; Male

Adult

Aged

Bone and Bones: PA, pathology

*Calcitonin: AD, administration & dosage

Calcitonin: TU, therapeutic use

Calcium: BL, blood

Drug Therapy, Combination

*Etidronate Disodium: AD, administration & dosage

Etidronate Disodium: TU, therapeutic use

Hypercalcemia: BL, blood

*Hypercalcemia: DT, drug therapy

Hypercalcemia: ET, etiology

Hypercalcemia: PA, pathology

*Immobilization

*Polyradiculoneuropathy: CO, complications

RN 7414-83-7 (Etidronate Disodium); 7440-70-2 (Calcium); 9007-12-9 (Calcitonin)

L158 ANSWER 30 OF 30 MEDLINE

AN 83148390 MEDLINE

DN 83148390

TI [Results of radium 224 therapy in ankylosing spondylitis (Strumpell-Marie-Bechterew disease)].

Ergebnisse einer Radium 224-Therapie der ankylosierenden Spondylitis (M. Strumpell-Marie-Bechterew).

AU Knop J; Stritzke P; Heller M; Redeker S; Crone-Munzebrock W

SO ZEITSCHRIFT FUR RHEUMATOLOGIE, (1982 Nov-Dec) 41 (6) 272-5.

Journal code: YOV. ISSN: 0301-6382.

CY GERMANY, WEST: Germany, Federal Republic of

DT Journal; Article; (JOURNAL ARTICLE)

LA German

FS Priority Journals

EM 198306

AB After an average of 5 years following therapy with Ra224, the concentration of Tc99m methyl diphosphonate (MDP) in the region of the sacroiliac joints and lumbar spine was measured in 15 patients with ankylosing spondylitis. The findings were supplemented by those of clinical, pathological, and roentgenological examinations. The concentration of MDP was normal in the sacroiliac joints in almost all the patients, but was raised in the lumbar spine in two-thirds. This is to be interpreted as indicating enhanced bone turnover, the difference from that in healthy subjects being highly significant (p less than 1). Increased ossification of the lumbar spine could be demonstrated roentgenologically in two-thirds of the patients. Differential blood count, blood sedimentation rate, and electrophoresis remained unchanged after therapy. However, in 60% of patients the mobility of the spine was the same or even improved; 46% felt better after Ra224 treatment than before it.

CT Check Tags: Female; Human; Male

Adult

Diphosphonates: ME, metabolism

English Abstract

Lumbosacral Region

Middle Age

Ossification, Heterotopic: DI, diagnosis

*Radium: TU, therapeutic use

Spine: ME, metabolism

*Spondylitis, Ankylosing: RT, radiotherapy

RN 1984-15-2 (methylene diphosphonate); 7440-14-4 (Radium)

CN 0 (Diphosphonates)